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L2 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:120425 HCAPLUS

DOCUMENT NUMBER: 134:305011

TITLE: Alpha-1-antitrypsin inhibits human immunodeficiency virus type 1

AUTHOR(S): Shapiro, Leland; Pott, Gregory B.; Ralston, Annemarie H.

CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases, University of Colorado Health Sciences Center, Denver, CO, 80262, USA

SOURCE: FASEB Journal (2001), 15(1), 115-122
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several observations suggest the existence of potent endogenous suppressors of human immunodeficiency virus type 1 (HIV-1) prodn., and inhibitors of serine proteases may participate in this effect. Alpha-1-antitrypsin (AAT) is the most abundant circulating serine protease inhibitor. Physiol. AAT concns. inhibited HIV-1 prodn. in chronically infected U1 monocytic cells, reduced virus replication in freshly infected peripheral blood mononuclear cells, and blocked infection of permissive HeLa cells. In U1 cells, AAT suppressed activation of the HIV-1-inducing transcription factor NF- κ B. Similar results were obtained using CE-2072, a synthetic inhibitor of host serine proteases. HIV-1 did not replicate in blood obtained from healthy volunteers, but marked replication was obsd. in blood from individuals with hereditary AAT deficiency. These results identify AAT as a candidate circulating HIV-1 inhibitor in vivo. Two different mechanisms of AAT-induced HIV-1 inhibition were identified, including reduced HIV-1 infectivity and blockade of HIV-1 prodn. A novel host-pathogen interaction is suggested, and an alternative strategy to treat HIV-1-related disease may be possible.

IT 208840-22-6, CE-2072

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(alpha-1-antitrypsin inhibits HIV-1)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:874195 HCAPLUS

DOCUMENT NUMBER: 134:29708

TITLE: Preparation of .alpha.-keto heterocycles as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert C.; Spruce, Lyle W.; Leimer, Axel H.; Cheronis, John C.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 5,807,829.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

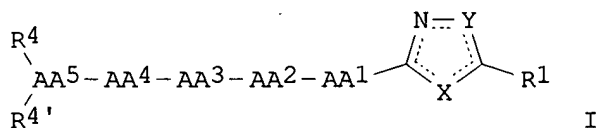
FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6159938	A	20001212	US 1997-859242	19970520
US 5618792	A	19970408	US 1994-345820	19941121
US 5807829	A	19980915	US 1996-761190	19961206
US 6037325	A	20000314	US 1998-69823	19980430

PRIORITY APPLN. INFO.:
 US 1994-345820 A2 19941121
 US 1996-761190 A2 19961206
 US 1996-698575 A1 19960815

OTHER SOURCE(S): MARPAT 134:29708
 GI



AB Heterocyclyl peptides I [AA1, AA2, AA3, AA4, AA5 are amino acid residues or mimetics or a direct bond; R4, R4' = COR5, CONHR5, SO2R5, CO2R5, CO-(C5-6)aryl-COR5, CH2R5 or R5, where R5 = H, alkyl, alkenyl, (un)substituted alkynyl, cycloalkyl, alkylcycloalkyl, aryl or arylalkyl optionally comprising 1-4 heteroatoms (N, O and S) and optionally substituted, or are absent or R4 and R4' together form a ring comprising 5-7 atoms selected from C, N, S and O; R1 = alkyl or alkenyl optionally substituted with 1-3 halo or hydroxy, alkylamino, cycloalkyl, aryl, etc.; Y, X = O, S, N or substituted N] were prepd. for inhibition of serine protease. Thus, N-acetyl-L-leucyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-[(5-phenyl-1,3,4-oxadiazol-2-yl)carbonyl]butyl]-L-leucinamide (CQ-0002) was prepd. and inhibited trypsin with $k_i = 0.62$ nM.

IT 208840-22-6P, Ce-2072

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of .alpha.-keto heterocycles as serine protease inhibitors)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:819473 HCAPLUS

DOCUMENT NUMBER: 134:5159

TITLE: Preparation of tripeptoid analogs as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert C.; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 107 pp., Cont-in-part of U. S. Ser. No. 761,190.
 CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6150334	A	20001121	US 1997-985201	19971204
US 5618792	A	19970408	US 1994-345820	19941121
US 5807829	A	19980915	US 1996-761190	19961206
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

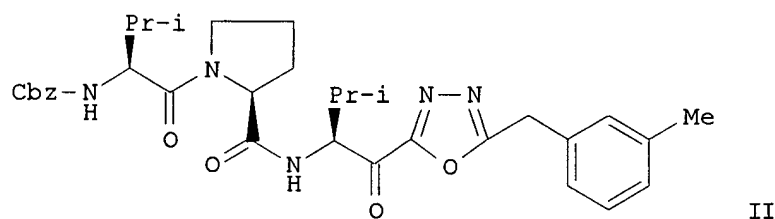
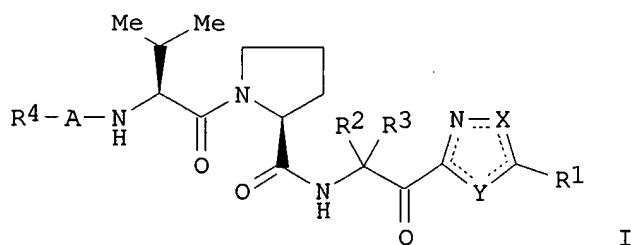
CN 1247542	A	20000315	CN 1997-180392	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
US 6001813	A	19991214	US 1998-90046	19980603
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-761190	A2	19961206
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761313	A	19961206
US 1996-762381	A	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

OTHER SOURCE(S):
GI

MARPAT 134:5159



AB Tripeptides I [X, Y = O, N, or S, provided that at least one of X or Y = N; R1 = (un)substituted (C5-12)aryl, (C5-12)arylalkyl, (C5-12)arylalkenyl, fused (C5-12)aryl-cycloalkyl, alkyl- or alkenyl-fused (C5-12)aryl-cycloalkyl optionally comprising one or more heteroatoms selected from N, S, or non-peroxide O; R2, R3 = H or alkyl; A = CO, NHCO, SO2, O2C, or CH2; R4 = H, alkyl, alkenyl, cycloalkyl, aryl, or arylalkyl (with provisos)] were prep'd. as serine protease inhibitors, including inhibitors of human neutrophil elastase. Thus, peptide I (Cbz = benzyloxycarbonyl) (CE-2072) was prep'd. and showed Ki = 0.025 nM for inhibition of elastase.

IT **208840-22-6P**, CE 2072

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tripeptoid analogs as serine protease inhibitors)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628160 HCAPLUS

DOCUMENT NUMBER: 133:232870

TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of viral infections and other conditions

INVENTOR(S): Shapiro, Leland

PATENT ASSIGNEE(S): The Trustees of University Technology Corp., USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052034	A2	20000908	WO 2000-US5558	20000303
WO 2000052034	A3	20010111		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-123167P P 19990305

US 1999-137795P P 19990603

OTHER SOURCE(S): MARPAT 133:232870

AB A method of treating and preventing viral infection is provided. In particular, a method of blocking viral infection facilitated by a serine proteolytic activity is disclosed, which consists of administering to a subject suffering or about to suffer from viral infection a therapeutically effective amt. of a compd. having a serine protease inhibitory or serpin activity. Among compds. are .alpha.1-antitrypsin (AAT), peptide derivs. from the carboxyterminal end of AAT, and man-made, synthetic compds. mimicking the action of such compds. The preferred viral infections include retroviral infection such as human immunodeficiency virus (HIV) infection. A method for treating other pathol. conditions mediated my a serine protease is also disclosed.

IT 208840-22-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors for treatment of viral infections and other conditions, and use with other agents)

L2 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628010 HCAPLUS

DOCUMENT NUMBER: 133:217681

TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of herpes virus infections

INVENTOR(S): Shapiro, Leland

PATENT ASSIGNEE(S): The Trustees of University Technology Corporation, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051625	A1	20000908	WO 2000-US5557	20000303

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-123167P P 19990305
US 1999-153942P P 19990915

OTHER SOURCE(S): MARPAT 133:217681

AB Compns. and methods of treating and preventing a viral infection are provided. A method of blocking a viral infection facilitated by a serine proteolytic (SP) activity is disclosed, which involves administering to a subject suffering or about to suffer from a viral infection a therapeutically effective amt. of a substance having serine protease inhibitory activity or serpin activity. Among the substances found to be useful are .alpha.1-antitrypsin (AAT), peptide derivs. from the carboxy terminal end of AAT and synthetic drugs mimicking the action of such substances. The invention is particularly well suited for checking a viral infection mediated by members of herpesviridae family.

IT 208840-22-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors and methods and compns. for treatment of herpes virus infections)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628009 HCAPLUS

DOCUMENT NUMBER: 133:217725

TITLE: Methods and compositions using serine protease inhibitors useful in inhibiting apoptosis, and therapeutic use thereof

INVENTOR(S): Shapiro, Leland

PATENT ASSIGNEE(S): The Trustees of University Technology Corporation, USA

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051624	A2	20000908	WO 2000-US6069	20000303
WO 2000051624	A3	20001228		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ,
DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-123167P P 19990305

AB A method is provided for treating an animal suffering a disease characterized by excessive apoptosis by administering a therapeutically effective amt. of at least one serine protease inhibitor and thereafter

monitoring a decrease in apoptosis. The inhibitor of the invention includes .alpha.1-antitrypsin or an .alpha.1-antitrypsin-like agent, including but not limited to oxidn.-resistant variants of .alpha.1-antitrypsin, and peptoids with antitrypsin activity. The diseases treatable by the invention include cancer, autoimmune disease, sepsis neurodegenerative disease, myocardial infarction, stroke, ischemia-reperfusion injury, toxin induced liver injury and AIDS. The method of the invention is also suitable for the prevention or amelioration of diseases characterized by excessive apoptosis.

IT 208840-22-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors for inhibiting apoptosis, and therapeutic use)

L2 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628008 HCAPLUS

DOCUMENT NUMBER: 133:217724

TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of nitric oxide-induced clinical conditions

INVENTOR(S): Shapiro, Leland

PATENT ASSIGNEE(S): The Trustees of University Technology Corp., USA

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051623	A2	20000908	WO 2000-US5556	20000303
WO 2000051623	A3	20001214		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6489308 B1 20021203 US 2000-518097 20000303

PRIORITY APPLN. INFO.: US 1999-123167P P 19990305

US 1999-156523P P 19990929

AB A method of treating and preventing diseases is provided. In particular, compns. and methods of blocking diseases assocd. with aberrant levels of nitric oxide and facilitated by a serine proteolytic activity are disclosed, which consist of administering to a subject a therapeutically effective amt. of a compd. having a serine protease inhibitory activity. Among effective compds. are .alpha.1-antitrypsin and synthetic drugs mimicking some or all of the actions of .alpha.1-antitrypsin.

IT 208840-22-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors for treatment of NO-induced diseases)

L2 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:47017 HCAPLUS

DOCUMENT NUMBER: 132:78559

TITLE: Preparation of heterocyclic compounds as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech Inc., USA

SOURCE: U.S., 107 pp., Cont.-in-part of U.S. 5,891,852.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

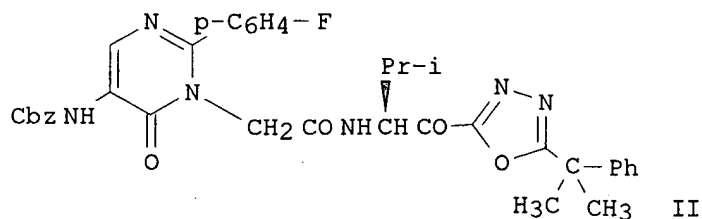
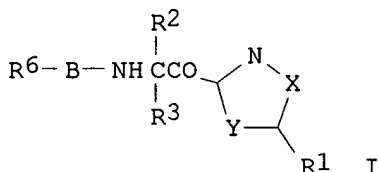
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6015791	A	20000118	US 1997-984881	19971204
US 5618792	A	19970408	US 1994-345820	19941121
US 5891852	A	19990406	US 1996-762381	19961206
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-762381	A2	19961206
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A	19961206
US 1996-761313	A	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

OTHER SOURCE(S): MARPAT 132:78559

GI



AB The present invention relates to a series of compds. of general structure I [X, Y = O, N, or S provided that at least one of X or Y = N; R1 = C5-12 aryl, C5-12 arylalkyl, or C5-12 arylalkenyl with at least one N, S, and O; R2, R3 = H or alkyl; B = S(O)₂ or C(O); R6 = heterocycles (generic structures given)] that are useful as serine protease inhibitors, including inhibitors for human neutrophil elastase. In an in vitro test for inhibition of elastase, the title compd. II shows the K_i value of 78.3. Compds. of the invention are useful in treating conditions such as adult respiratory distress syndrome, septic shock, and multiple organ failure.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic compds. as serine protease inhibitors)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:794318 HCAPLUS

DOCUMENT NUMBER: 132:23197

TITLE: Preparation of N-substituted prolinyl peptide analogs as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech Inc., USA

SOURCE: U.S., 107 pp., Cont.-in-part of U.S. 5,869,455.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6001811	A	19991214	US 1997-984884	19971204

US 5618792	A	19970408	US 1994-345820	19941121
US 5869455	A	19990209	US 1996-761313	19961206
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

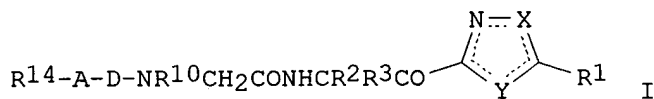
CN 1247542	A	20000315	CN 1997-180392	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
US 6037325	A	20000314	US 1998-69823	19980430
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-761313	A2	19961206
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A	19961206
US 1996-762381	A	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
WO 1997-US21636	W	19971205

OTHER SOURCE(S): MARPAT 132:23197

GI



AB Proline analogs I [X, Y = O, S, N or substituted N; R¹ = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, aryl, arylalkyl, arylalkenyl, etc.; R², R³ = H, (un)substituted alkyl or alkenyl, -RCOR', -RCO₂R', -RNR'R''R⁰, or -RCONR'R'', where R is alkyl or alkenyl and R', R'', and R⁰ are H, alkyl, alkenyl, cycloalkyl, aryl, cycloalkyl, etc.; R¹⁰ = aryl, arylalkyl, arylalkenyl, cycloalkyl, alkylcycloalkyl, etc.; D is a direct bond or an amino acid selected from proline, isoleucine, cyclohexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, NHCO, SO₂, OCO, CH₂; R¹⁴ = H, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, etc.] were prepd. as serine

protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1(S)-[[5-(3-methylbenzyl)-1,3,5-oxadiazolyl]carbonyl]-2-methylpropyl]-L-prolinamide was prepd. and showed $K_i = 0.025$ nM for inhibition of human neutrophil elastase.

IT 208840-22-6P, CE 2072

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of prolinyl peptide analogs as serine protease inhibitors)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:779215 HCAPLUS

DOCUMENT NUMBER: 132:36032

TITLE: Preparation of prolinyl peptide analogs as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech Inc., USA

SOURCE: U.S., 110 pp., Cont.-in-part of U.S. 5,801,148.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

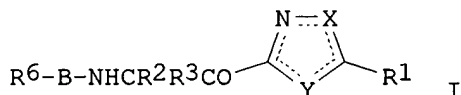
FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5998379	A	19991207	US 1997-985056	19971204
US 5618792	A	19970408	US 1994-345820	19941121
US 5801148	A	19980901	US 1996-771317	19961206
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
US 6037325	A	20000314	US 1998-69823	19980430
US 6100238	A	20000808	US 1998-89587	19980603
NO 9902734	A	19990802	NO 1999-2734	19990604
PRIORITY APPLN. INFO.:				
			US 1994-345820	A2 19941121
			US 1996-771317	A2 19961206
			US 1996-698575	A1 19960815
			US 1996-760916	A 19961206
			US 1996-761190	A 19961206
			US 1996-761313	A 19961206

US 1996-762381 A 19961206
 US 1997-984881 A 19971204
 US 1997-984884 A 19971204
 US 1997-985056 A 19971204
 US 1997-985201 A 19971204
 US 1997-985298 A 19971204
 WO 1997-US21636 W 19971205

OTHER SOURCE(S): MARPAT 132:36032
 GI



AB Proline analogs I [X, Y = O, S, N or substituted N; R1 = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, aryl, arylalkyl, arylalkenyl, etc.; R2, R3 = H, (un)substituted alkyl or alkenyl, -RCOR', -RCO2R', -RNR'R''R0, or -RCONR'R'', where R is alkyl or alkenyl and R', R'', and R0 are H, alkyl, alkenyl, cycloalkyl, aryl, cycloalkyl, etc.; B = SO2, CO, OCO, CH2CO; R6 = aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, or R14-A-D-NR7CHR8-, where R7R8 is o-(CH2)nC6H4(CH2)m (m, n = 0, 1), D is a direct bond or an amino acid selected from proline, isoleucine, cyclohexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, NHCO, SO2, OCO, CH2; R14 = H, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, etc.] were prepd. as serine protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1(S)-[[5-(3-methylbenzyl)-1,3,5-oxadiazolyl]carbonyl]-2-methylpropyl]-L-prolinamide was prepd. and showed Ki = 0.025 nM for inhibition of human neutrophil elastase.

IT 208840-22-6P, CE 2072

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of prolinyl peptide analogs as serine protease inhibitors)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:691089 HCAPLUS

DOCUMENT NUMBER: 131:310839

TITLE: Preparation of heterocyclyl peptide derivatives as cysteine protease inhibitors

INVENTOR(S): Spruce, Lyle W.; Gyorkos, Albert C.; Cheronis, John C.; Goodfellow, Val S.; Leimer, Axel H.; Young, John M.; Gerrity, James I.

PATENT ASSIGNEE(S): Cortech Inc., USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

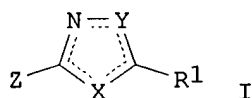
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954317	A1	19991028	WO 1999-US8501	19990423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6004933	A	19991221	US 1998-65258	19980423
CA 2329712	AA	19991028	CA 1999-2329712	19990423
AU 9939651	A1	19991108	AU 1999-39651	19990423
AU 750369	B2	20020718		
PRIORITY APPLN. INFO.:			US 1998-65258	A 19980423
			WO 1999-US8501	W 19990423
OTHER SOURCE(S):			MARPAT 131:310839	
GI				



AB Compds. I (Z is a cysteine protease binding moiety; R1 = alkyl or alkenyl optionally substituted by halo or hydroxy, alkylamino, dialkylamino, alkyldialkylamino, or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, aryl, arylalkyl, or arylalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted by halo, cyano, nitro, amino, alkyl, aryl, etc.; Y, X = O, S, or optionally substituted N) were prepd. as cysteine protease inhibitors. Thus, N-[1(S)-[[5-(3-methylbenzyl)-1,3,4-oxadiazol-2-yl]carbonyl]-2-methylpropyl]-L-phenylalaninamide-(3R)-(isobutyl)succinic acid, prepd. from 3(S)-[(benzyloxycarbonyl)amino]-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, 4-methylvaleric acid, (S)-(-)-4-benzyl-2-oxazolidinone, tert-Bu bromoacetate, tert-butyl-(3R)-3-(isobutyl)succinate, and L-phenylalanine Me ester hydrochloride, showed K_i = 85, 3,000, and .apprx.100 nM for inhibition of papain, cathepsin B, and cathepsin L, resp.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl peptide derivs. as cysteine protease inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:425234 HCAPLUS

DOCUMENT NUMBER: 131:252079

TITLE: Biochemical characterization of .alpha.-ketooxadiazole inhibitors of elastases

AUTHOR(S): Wieczorek, Maciej; Gyorkos, Albert; Spruce, Lyle W.; Ettinger, Anna; Ross, Sherman E.; Kroona, Heather S.; Burgos-Lepley, Carmen E.; Bratton, Larry D.; Drennan, Tyler S.; Garnert, Douglas L.; Von Burg, Gregory; Pilkington, Carolyn G.; Cheronis, John C.

CORPORATE SOURCE: Cortech, Inc., Denver, CO, 80221, USA

SOURCE: Archives of Biochemistry and Biophysics (1999), 367(2), 193-201
CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of .alpha.-ketooxadiazole compds. was prepd. and evaluated in vitro as potential inhibitors of human neutrophil elastase (HNE), proteinase-3 (PR-3), and porcine pancreatic elastase (PPE). Several compds. have been found to be very potent, fast, reversible, and selective inhibitors of HNE with Ki values below 100 pM. The highest kon value exceeded 107 M⁻¹ s⁻¹. Some .alpha.-ketooxadiazoles were also very effective against PR-3 and PPE with Ki values in the range of 5-10 nM and 0.1-2 nM, resp. The two rings, 1,2,4- and 1,3,4-oxadiazole, are amenable to substitutions, extending the P' side of the inhibitor and allowing addnl. binding interactions at S' subsites of the enzyme. Nonpeptidic HNE inhibitors contg. the oxadiazole heterocycle displayed promising oral bioavailability. (c) 1999 Academic Press.

IT 208840-22-6P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(biochem. characterization of .alpha.-ketooxadiazole inhibitors of elastases)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:231191 HCAPLUS

DOCUMENT NUMBER: 130:252684

TITLE: Preparation of fused cycloheptane azole heterocyclic peptoids as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 61 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891852	A	19990406	US 1996-762381	19961206
US 5618792	A	19970408	US 1994-345820	19941121
CA 2205198	AA	19960530	CA 1995-2205198	19951117
CN 1170414	A	19980114	CN 1995-196952	19951117
ES 2145936	T3	20000716	ES 1995-940031	19951117
ZA 9509819	A	19960530	ZA 1995-9819	19951120
TW 474924	B	20020201	TW 1995-84112388	19951120
IL 116078	A1	19991231	IL 1995-116078	19951121

US 5874585	A	19990223	US 1996-698575	19960815
US 6015791	A	20000118	US 1997-984881	19971204
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
BR 9713684	A	20000328	BR 1997-13684	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A	19961206
US 1996-761313	A	19961206
US 1996-762381	A2	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl, alkenyl (un)substituted with halo or OH; alkynyl, alkyl-CO2Me, dialkylamino, alkylalkylamino; cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally contg. .gtoreq.1 N, S, O atoms, and optionally substituted; R2, R3, R21, R31 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine, amidine; B = SO2, CO; R6 = fused cycloheptane ring system Q1-Q3; R13, R15 = independently H, alkyl, halo, alkoxy, carboalkoxy, cycloalkoxy, carboxyl, alkylthio, amino, alkylamino or dialkylamino; aryl, fused aryl, cycloalkyl optionally contg. .gtoreq.1 O,

N, S atoms, and optionally substituted with halo or alkyl; R14 = H, aminoalkyl, alkenyl; (un)substituted cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally contg. .gtoreq.1 N, O, S atoms] and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. R14 = H, aminoalkyl, alkenyl; cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally contg. .gtoreq.1 N, O, S atoms, and optionally substituted with alkyl, halo, alkoxy, amino, alkylamino, dialkylamino, carboxy, alkenyl, alkynyl, haloalkoxy, carboalkoxy, alkylcarboxamido, aryl, arylcarboxamido, alkylthio, haloalkylthio;. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of hexahydroazepinoindolecarboxylic acid II (Fmoc = 9-fluorenylmethoxycarbonyl) with amino alc. III (prepn. given), followed by Swern oxidn. and deprotection gave desired title compd. IV. IV inhibited human neutrophil elastase with $K_i = 10.0$ nM.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of fused cycloheptane azole heterocyclic peptoids as serine protease inhibitors)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:104503 HCAPLUS

DOCUMENT NUMBER: 130:125411

TITLE: Preparation of N-substituted derivatives of azole heterocyclic peptoids as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 345,820. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5869455	A	19990209	US 1996-761313	19961206
US 5618792	A	19970408	US 1994-345820	19941121
CA 2205198	AA	19960530	CA 1995-2205198	19951117
CN 1170414	A	19980114	CN 1995-196952	19951117
ES 2145936	T3	20000716	ES 1995-940031	19951117
ZA 9509819	A	19960530	ZA 1995-9819	19951120
TW 474924	B	20020201	TW 1995-84112388	19951120
IL 116078	A1	19991231	IL 1995-116078	19951121
US 5874585	A	19990223	US 1996-698575	19960815
US 6001811	A	19991214	US 1997-984884	19971204
WO 9824806	A2	19980611	WO 1997-US21636	19971205

WO 9824806 A3 19981015

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9855894 A1 19980629 AU 1998-55894 19971205

AU 734615 B2 20010621

EP 954526 A2 19991110 EP 1997-952232 19971205

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

CN 1247542 A 20000315 CN 1997-180392 19971205

BR 9713684 A 20000328 BR 1997-13684 19971205

JP 2001507679 T2 20010612 JP 1998-525656 19971205

JP 3220169 B2 20011022

JP 2001192398 A2 20010717 JP 2000-197432 19971205

US 6037325 A 20000314 US 1998-69823 19980430

NO 9902734 A 19990802 NO 1999-2734 19990604

PRIORITY APPLN. INFO.:

US 1994-345820 A2 19941121

US 1996-698575 A1 19960815

US 1996-760916 A 19961206

US 1996-761190 A 19961206

US 1996-761313 A2 19961206

US 1996-762381 A 19961206

US 1996-771317 A 19961206

US 1997-984881 A 19971204

US 1997-984884 A 19971204

US 1997-985056 A 19971204

US 1997-985201 A 19971204

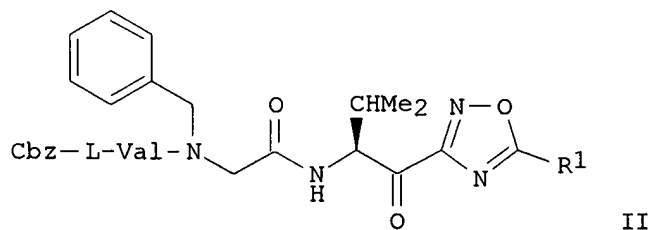
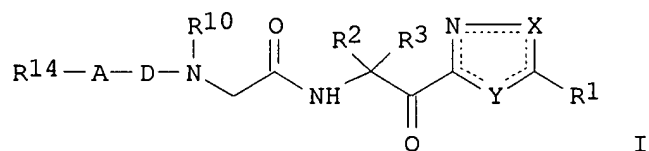
US 1997-985298 A 19971204

JP 1998-525656 A3 19971205

WO 1997-US21636 W 19971205

OTHER SOURCE(S): MARPAT 130:125411

GI



AB The present invention relates to certain substituted oxadiazole,

thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkylalkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally contg. 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine or amidine; R10 = C5-6 aryl, C5-6 arylalkyl, C5-6 arylalkenyl, cycloalkyl, arylcycloalkyl optionally contg. 1 or more heteroatoms N, S, O, and optionally substituted; D = bond, CO, amino acid residue; A = bond, CO, NHCO, SO2, O2C, CH2; R14 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally contg. 1 or more heteroatoms N, O, S, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, oxadiazolyl tripeptoid II (R1 = CH2C6H4CF3-3; Cbz = PhCH2O2C) inhibited human neutrophil elastase with Ki = 0.98 nM.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of azole heterocyclic peptoids as serine protease inhibitors)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:56366 HCAPLUS

DOCUMENT NUMBER: 130:125406

TITLE: Preparation of azole heterocyclic peptoids containing keto or diketo ring systems as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 67 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861380	A	19990119	US 1996-760916	19961206
US 5618792	A	19970408	US 1994-345820	19941121
CA 2205198	AA	19960530	CA 1995-2205198	19951117
CN 1170414	A	19980114	CN 1995-196952	19951117
ES 2145936	T3	20000716	ES 1995-940031	19951117
ZA 9509819	A	19960530	ZA 1995-9819	19951120
TW 474924	B	20020201	TW 1995-84112388	19951120

IL 116078	A1	19991231	IL 1995-116078	19951121
US 5874585	A	19990223	US 1996-698575	19960815
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
BR 9713684	A	20000328	BR 1997-13684	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
US 6001814	A	19991214	US 1998-90274	19980603
NO 9902734	A	19990802	NO 1999-2734	19990604
US 2002119985	A1	20020829	US 2001-927832	20010810
US 2002119998	A1	20020829	US 2001-991286	20011116

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A	19961206
US 1996-761313	A	19961206
US 1996-762381	A	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

OTHER SOURCE(S): MARPAT 130:125406

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkylalkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally contg. 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = R'2, R'3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl,

alkylthio, alkylguanidine, dialkylguanidine or amidine; R11, R12 and E together form a monocyclic or bicyclic ring comprising 5-10 atoms selected from C, N, S, and O; said ring contg. 1 or more keto groups; and optionally substituted with halo, cyano, nitro, haloalkyl, amino, aminoalkyl, dialkylamino, alkyl, alkenyl, alkynyl, alkoxy, carboxyl, etc; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, (C5-12 arylalkyl)OCONH, C5-12 arylalkenyl optionally contg. 1 or more heteroatoms N, S, O, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of valine-derived oxadiazole II (R1 = CH₂C₆H₄Me-3) (prepn. given) with III (Cbz = PhCH₂O₂C), followed by oxidn. of the secondary alc. to the corresponding ketone gave oxadiazole peptide deriv. IV. IV inhibited human neutrophil elastase with K_i = 0.21 nM.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of azole heterocyclic peptoids as serine protease inhibitors)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 19 HCAPLUS, COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:721721 HCAPLUS

DOCUMENT NUMBER: 130:4087

TITLE: Preparation of substituted oxadiazole peptide derivatives as cysteine protease inhibitors

INVENTOR(S): Spruce, Lyle W.; Gyorkos, Albert C.; Cheronis, John C.; Goodfellow, Val S.; Leimer, Axel H.; Young, John M.; Gerrity, James Ivan

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849190	A2	19981105	WO 1998-US8259	19980424
WO 9849190	A3	19990218		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

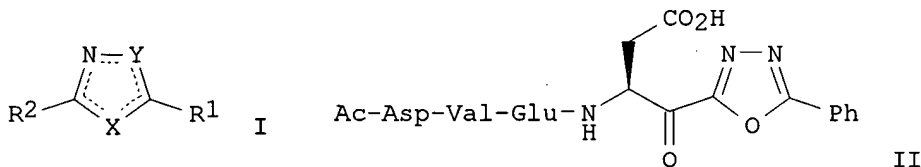
AU 9871556 A1 19981124 AU 1998-71556 19980424
EP 979242 A2 20000216 EP 1998-918677 19980424

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRIORITY APPLN. INFO.:

US 1997-44819P P 19970425
US 1998-65258 A 19980423
WO 1998-US8259 W 19980424

OTHER SOURCE(S): MARPAT 130:4087
GI



AB The present invention relates to cysteine protease inhibitors I [Z = cysteine protease binding moiety, being a carbonyl contg. group, preferably an aminocarbonyl contg. group, wherein the carbon of the heterocycle is attached directly to the carbonyl group of Z; X, Y = independently O, S or N, where N is optionally substituted with alkyl or alkenyl optionally substituted with 1-3 halo atoms; (C5-C6)aryl, arylalkyl or arylalkenyl optionally comprising 1-3 heteroatoms selected from N, O and S, and optionally substituted with halo, cyano, nitro, haloalkyl, amino, aminoalkyl, dialkylamino, alkyl, alkenyl, alkynyl, alkoxy, haloalkoxy, carboxyl, carboalkoxy, alkylcarboxamide, arylcarboxamide, alkylthio or haloalkylthio; provided that at least one of Y or X = N; R1 = alkyl or alkenyl (un)substituted with 1-3 halo or hydroxy groups; alkylamino, dialkylamino, alkylalkylamino; cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, (C5-12)aryl, (C5-12)arylalkyl, (C5-12)arylalkenyl optionally comprising 1-4 heteroatoms N, O and S, and (un)substituted with halo, cyano, NO₂, haloalkyl, amino, aminoalkyl, dialkylamino, alkyl, alkenyl, alkynyl, alkoxy, haloalkoxy, carboxyl, carboalkoxy, alkylcarboxamide, (C5-6)aryl, O(C5-6)aryl, arylcarboxamide, alkylthio or haloalkylthio]. Thus, oxadiazolyl peptide II, prepd. in 5 steps from Cbz-Asp(OCMe₃)-OH, Ac-Asp(OCMe₃)-Val-Gly(OCMe₃)-OH, and 2-phenyl-1,3,4-oxadiazole, inhibited caspase 3 with IC₅₀ .ltoreq. 0.1 .mu.M and caspase 6 with IC₅₀ = 6.7 .mu.M. Related oxadiazolyl peptides were prepd. and tested for inhibition of caspase 8, caspase 1, granzyme, papain, cathepsin B, cathepsin L, and gingipain R.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted oxadiazole peptide derivs. as cysteine protease inhibitors)

L2 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:604649 HCAPLUS

DOCUMENT NUMBER: 129:231017

TITLE: Preparation of azole heterocyclic peptoids as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA

SOURCE: U.S., 62 pp., Cont.-in-part of U.S. 5,618,792.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 18
 PATENT INFORMATION:

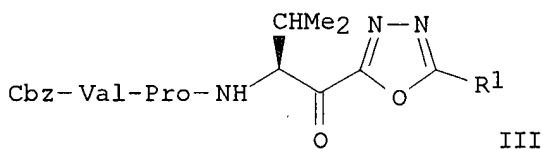
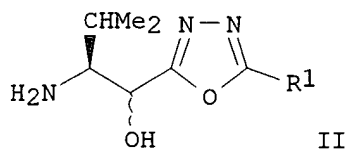
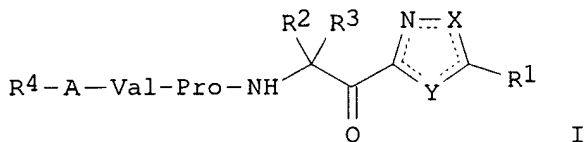
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5807829	A	19980915	US 1996-761190	19961206
US 5618792	A	19970408	US 1994-345820	19941121
CA 2205198	AA	19960530	CA 1995-2205198	19951117
CN 1170414	A	19980114	CN 1995-196952	19951117
ES 2145936	T3	20000716	ES 1995-940031	19951117
ZA 9509819	A	19960530	ZA 1995-9819	19951120
TW 474924	B	20020201	TW 1995-84112388	19951120
IL 116078	A1	19991231	IL 1995-116078	19951121
US 5874585	A	19990223	US 1996-698575	19960815
US 6159938	A	20001212	US 1997-859242	19970520
US 6150334	A	20001121	US 1997-985201	19971204
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
BR 9713684	A	20000328	BR 1997-13684	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
US 6001813	A	19991214	US 1998-90046	19980603
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A2	19961206
US 1996-761313	A	19961206
US 1996-762381	A	19961206
US 1996-771317	A	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

OTHER SOURCE(S): MARPAT 129:231017

GI



AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = O, N, S; at least one of X or Y = N; R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-CO2Me, dialkylamino, alkylalkylamino; or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl optionally contg. 1 or more heteroatoms N, S, O, and optionally substituted; R2, R3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guanidine, carboalkoxy, OH, haloalkyl, alkylthio, alkylguanidine, dialkylguanidine or amidine; A = bond, CO, NHCO, SO2, O2C, CH2, amino acid residue; R4 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally contg. 1 or more heteroatoms N, O, S, and optionally substituted], and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of valine-derived oxadiazole II (R1 = CH2C6H4Me-3) (prepn. given) with Cbz-Val-Pro-OH (Cbz = PhCH2O2C), followed by oxidn. of the secondary alc. to the corresponding ketone gave oxadiazole peptide deriv. III. III inhibited human neutrophil elastase with Ki = 0.025 nM.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of azole heterocyclic peptoids as serine protease inhibitors)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:585365 HCAPLUS

DOCUMENT NUMBER: 129:216917

TITLE: preparation of proline analog peptides as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

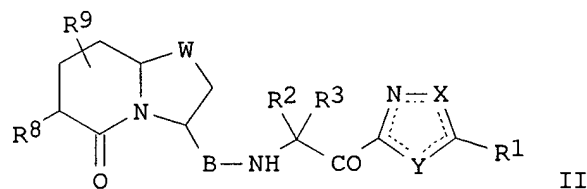
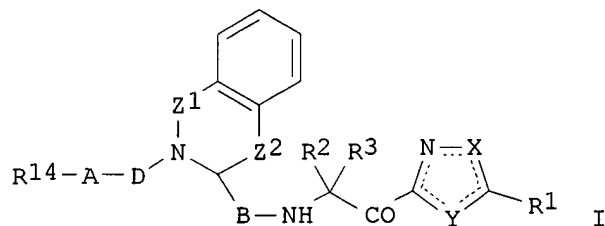
PATENT ASSIGNEE(S): Cortech, Inc., USA
 SOURCE: U.S., 62 pp., Cont.-in-part of U. S. 5,618,792.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 18
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5801148	A	19980901	US 1996-771317	19961206
US 5618792	A	19970408	US 1994-345820	19941121
CA 2205198	AA	19960530	CA 1995-2205198	19951117
CN 1170414	A	19980114	CN 1995-196952	19951117
ES 2145936	T3	20000716	ES 1995-940031	19951117
ZA 9509819	A	19960530	ZA 1995-9819	19951120
TW 474924	B	20020201	TW 1995-84112388	19951120
IL 116078	A1	19991231	IL 1995-116078	19951121
US 5874585	A	19990223	US 1996-698575	19960815
US 5998379	A	19991207	US 1997-985056	19971204
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1247542	A	20000315	CN 1997-180392	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
JP 2001192398	A2	20010717	JP 2000-197432	19971205
US 6037325	A	20000314	US 1998-69823	19980430
US 6100238	A	20000808	US 1998-89587	19980603
NO 9902734	A	19990802	NO 1999-2734	19990604

PRIORITY APPLN. INFO.:

US 1994-345820	A2	19941121
US 1996-698575	A1	19960815
US 1996-760916	A	19961206
US 1996-761190	A	19961206
US 1996-761313	A	19961206
US 1996-762381	A	19961206
US 1996-771317	A2	19961206
US 1997-984881	A	19971204
US 1997-984884	A	19971204
US 1997-985056	A	19971204
US 1997-985201	A	19971204
US 1997-985298	A	19971204
JP 1998-525656	A3	19971205
WO 1997-US21636	W	19971205

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AB Proline analog peptides I and II [X, Y = O, N, S; R1 = alkyl, alkenyl, alkynyl, dialkylamino, etc.; R2, R3 = H, alkyl, alkylthio, alkylthioalkyl, etc.; B = SO₂, CO; Z1, Z2 = direct bond or CH₂; D = direct bond or certain amino acid residues; A = CO, NHCO, SO₂, OCO, O₂CNH, CH₂; R14 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, dialkylamino, amino; R9 = H, alkyl, halo] or their pharmaceutically acceptable salts were prepd. as serine protease inhibitors. Thus, (benzyloxycarbonyl)-L-valyl-N-[1-[2-[5-(3-methylbenzyl)-1,3,4-oxadiazolyl]carbonyl]-2-(S)-methylprolyl]-L-prolinamide, prepd. from 3-(S)-[(benzyloxycarbonyl)amino]-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, and Cbz-Val-Pro-OH, showed inhibition activity $K_i = 0.025$ nM.

IT 208840-22-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline analog peptides as serine protease inhibitors)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:394350 HCAPLUS

DOCUMENT NUMBER: 129:68032

TITLE: Preparation of oxadiazole peptide analogs as serine protease inhibitors

INVENTOR(S): Gyorkos, Albert; Spruce, Lyle W.

PATENT ASSIGNEE(S): Cortech, Inc., USA; Gyorkos, Albert; Spruce, Lyle W.

SOURCE: PCT Int. Appl., 187 pp.

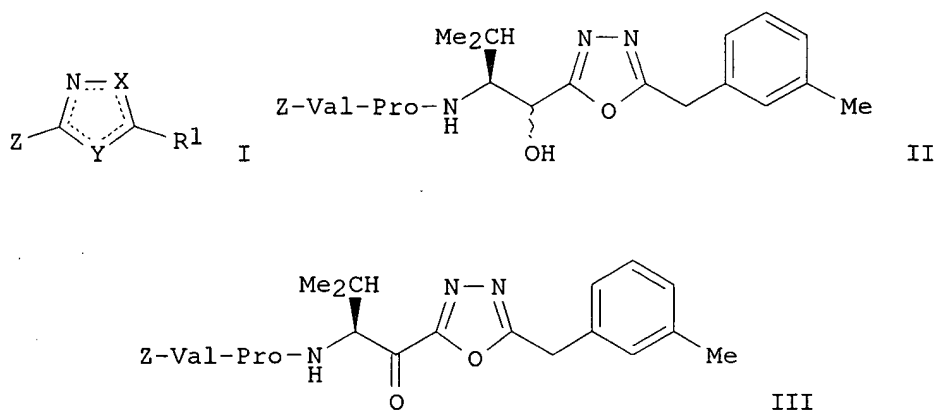
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824806	A2	19980611	WO 1997-US21636	19971205
WO 9824806	A3	19981015		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5801148	A	19980901	US 1996-771317	19961206
US 5807829	A	19980915	US 1996-761190	19961206
US 5861380	A	19990119	US 1996-760916	19961206
US 5869455	A	19990209	US 1996-761313	19961206
US 5891852	A	19990406	US 1996-762381	19961206
US 5998379	A	19991207	US 1997-985056	19971204
US 6001811	A	19991214	US 1997-984884	19971204
US 6015791	A	20000118	US 1997-984881	19971204
US 6150334	A	20001121	US 1997-985201	19971204
AU 9855894	A1	19980629	AU 1998-55894	19971205
AU 734615	B2	20010621		
EP 954526	A2	19991110	EP 1997-952232	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9713684	A	20000328	BR 1997-13684	19971205
JP 2001507679	T2	20010612	JP 1998-525656	19971205
JP 3220169	B2	20011022		
NO 9902734	A	19990802	NO 1999-2734	19990604
PRIORITY APPLN. INFO.:				
			US 1996-760916	A 19961206
			US 1996-761190	A 19961206
			US 1996-761313	A 19961206
			US 1996-762381	A 19961206
			US 1996-771317	A 19961206
			US 1997-984881	A 19971204
			US 1997-984884	A 19971204
			US 1997-985056	A 19971204
			US 1997-985201	A 19971204
			US 1997-985298	A 19971204
			US 1994-345820	A2 19941121
			WO 1997-US21636	W 19971205
OTHER SOURCE(S): MARPAT 129:68032				
GI				



AB The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptide analogs I [X, Y = independently O, S, (un)substituted N; Z = serine protease binding moiety, preferably a human neutrophil elastase binding moiety; R₁ = (un)substituted alkyl, alkenyl, alkynyl; OH, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkenyl, alkylcycloalkenyl, alkenylcycloalkenyl, C5-12 aryl, C5-12 arylalkyl, C5-12 arylalkenyl, fused C5-12 arylcycloalkyl, alkyl fused C5-12 arylcycloalkyl] which are useful as inhibitors of serine proteases. Thus, Swern oxidn. of reduced pseudopeptide II (Z = PhCH₂O₂C), prepd. in 8 steps from 3S-(benzyloxycarbonylamino)-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, and Z-Val-Pro-OH, gave 74% desired oxadiazole III. III inhibited human neutrophil elastase with IC₅₀ = 0.025 nM in an in vitro assay.

IT **208840-22-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oxadiazole peptide analogs as serine protease and human neutrophil elastase inhibitors)

=> d 13 ibib abs hitrn 1-2

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628010 HCAPLUS

DOCUMENT NUMBER: 133:217681

TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of **herpes** virus infections

INVENTOR(S): Shapiro, Leland

PATENT ASSIGNEE(S): The Trustees of University Technology Corporation, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051625	A1	20000908	WO 2000-US5557	20000303
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-123167P P 19990305

US 1999-153942P P 19990915

OTHER SOURCE(S): MARPAT 133:217681

AB Compns. and methods of treating and preventing a viral infection are provided. A method of blocking a viral infection facilitated by a serine proteolytic (SP) activity is disclosed, which involves administering to a subject suffering or about to suffer from a viral infection a therapeutically effective amt. of a substance having serine protease inhibitory activity or serpin activity. Among the substances found to be useful are .alpha.1-antitrypsin (AAT), peptide derivs. from the carboxy terminal end of AAT and synthetic drugs mimicking the action of such substances. The invention is particularly well suited for checking a viral infection mediated by members of **herpesviridae** family.

IT 208840-22-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors and methods and compns. for treatment of **herpes** virus infections)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628008 HCAPLUS

DOCUMENT NUMBER: 133:217724

TITLE: Inhibitors of serine protease activity, and methods and compositions for treatment of nitric oxide-induced clinical conditions

INVENTOR(S): Shapiro, Leland
 PATENT ASSIGNEE(S): The Trustees of University Technology Corp., USA
 SOURCE: PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051623	A2	20000908	WO 2000-US5556	20000303
WO 2000051623	A3	20001214		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6489308	B1	20021203	US 2000-518097	20000303
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PRIORITY APPLN. INFO.: US 1999-123167P P 19990305
 US 1999-156523P P 19990929

AB A method of treating and preventing diseases is provided. In particular, compns. and methods of blocking diseases assocd. with aberrant levels of nitric oxide and facilitated by a serine proteolytic activity are disclosed, which consist of administering to a subject a therapeutically effective amt. of a compd. having a serine protease inhibitory activity. Among effective compds. are .alpha.1-antitrypsin and synthetic drugs mimicking some or all of the actions of .alpha.1-antitrypsin.

IT **208840-22-6**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serine protease inhibitors for treatment of NO-induced diseases)

=> d 15 ibib abs 1-1

L5 ANSWER 1 OF 1 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001119156 EMBASE
TITLE: Molecular targets for antiviral agents.
AUTHOR: De Clercq E.
CORPORATE SOURCE: E. De Clercq, Rega Institute for Medical Research, K. U.
Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium.
erik.declercq@rega.kuleuven.ac.be
SOURCE: Journal of Pharmacology and Experimental Therapeutics,
(2001) 297/1 (1-10).
Refs: 39
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB There are a number of virus-specific processes within the virus replicative cycle or virus-infected cell that have proven to be attractive targets for chemotherapeutic intervention, i.e., virus adsorption and entry into the cells, reverse (RNA .fwdarw. DNA) transcription, viral DNA polymerization, and cellular enzymatic reactions that are associated with viral DNA and RNA synthesis and viral mRNA maturation (i.e., methylation). A variety of chemotherapeutic agents, both nucleoside (and nucleotide) and non-nucleoside entities, have been identified that specifically interact with these viral targets, that selectively inhibit virus replication, and that are either used or considered for clinical use in the treatment of virus infections in humans. Their indications encompass virtually all major human viral pathogens, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), **herpes** simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV), human papilloma virus (HPV), orthomyxoviruses (influenza A and B), paramyxoviruses [e.g., respiratory syncytial virus (RSV)] and hemorrhagic fever viruses (such as Ebola virus).

=> d 117 ibib abs 1-23

L17 ANSWER 1 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2001-091194 [10] WPIDS
 DOC. NO. CPI: C2001-026809
 TITLE: Benzothiazinone and benzoxazinone protein kinase inhibitors, used e.g. to affect angiogenesis and treat hyperproliferative disorders, cancers, arthritis, atherosclerosis, psoriasis, hemangioma, edema, stroke and diabetes.
 DERWENT CLASS: B02
 INVENTOR(S): ARNOLD, L D; CALDERWOOD, D; DE VEGA, M J P; FERNANDEZ, I F; MATINEZ, J L O; PASCUAL, B G; RAFFERTY, P; GONZALES, P B; ORTEGO, M J L; PEREZ DE VEGA, M J; GONZALEZ PASCUAL, B; ORTEGO MARTINEZ, J L; GONZALES, B P; ORTEGO, J L M; ORTEGO MARTINEZ, J L
 PATENT ASSIGNEE(S): (BADI) BASF AG; (KNOL) KNOLL GMBH
 COUNTRY COUNT: 43
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000075139	A2	20001214	(200110)*	EN	183
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BG BR CA CN CZ HR HU ID IL IN JP KR MX NO NZ PL RU SG SK TR UA					
US ZA					
AU 2000051790	A	20001228	(200119)		
EP 1181282	A2	20020227	(200222)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 2001005899	A	20020130	(200223)		
BR 2000011063	A	20020416	(200234)		
CZ 2001004244	A3	20020717	(200260)		
JP 2003501429	W	20030114	(200306)		212

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000075139	A2	WO 2000-US15324	20000602
AU 2000051790	A	AU 2000-51790	20000602
EP 1181282	A2	EP 2000-936476	20000602
		WO 2000-US15324	20000602
NO 2001005899	A	WO 2000-US15324	20000602
		NO 2001-5899	20011203
BR 2000011063	A	BR 2000-11063	20000602
		WO 2000-US15324	20000602
CZ 2001004244	A3	WO 2000-US15324	20000602
		CZ 2001-4244	20000602
JP 2003501429	W	WO 2000-US15324	20000602
		JP 2001-502421	20000602

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000051790 A	Based on	WO 200075139
EP 1181282	A2 Based on	WO 200075139
BR 2000011063 A	Based on	WO 200075139
CZ 2001004244 A3	Based on	WO 200075139
JP 2003501429 W	Based on	WO 200075139

PRIORITY APPLN. INFO: US 1999-137410P 19990603

AN 2001-091194 [10] WPIDS

AB WO 200075139 A UPAB: 20010220

NOVELTY - Benzothiazinone and benzooxazoinone compounds (I) and their physiologically acceptable salts are new.

DETAILED DESCRIPTION - A method of inhibiting one or more protein kinase activities comprising administration of a compound of formula (I) is new:

ring A = optionally substituted;

Q = -N= or -CR2=;

X = S, O or NOR3;

Y = O, S, SO or SO2;

R, R1 = H or an unsubstituted aliphatic, aromatic or aralkyl group;

R2 = H, or a substituent;

R3 = H or C(O)R4;

R4 = optionally substituted aliphatic, aromatic or aralkyl group;

and

n = 0-1.

INDEPENDENT CLAIMS are included for:

(1) treatment of a hyperproliferative disorder comprising administration of a compound of formula (I);

(2) a method of affecting angiogenesis comprising administration of a compound of formula (I);

(3) a method of inhibiting vascular hyperpermeability or the production of edema comprising administration of a compound of formula (I);

(4) compounds of formula (Ia) and their salts:

R4 = an optionally substituted aliphatic or aromatic group;

When X = S or NOR3, R = an optionally substituted aromatic or aralkyl group and R1 = H or an optionally substituted aliphatic group;

when X = O and n = 0, R1 = H or an optionally substituted aliphatic group and R is an optionally substituted aromatic or aralkyl group, provided that R is not thiophenyl, **benzoxadiazolyl**, 3-furanyl, 3-pyridinyl or a group of formula (a), where R14 is H, CF3, phenyl, OCH3, O-phenyl, NO2, or OC(O)CH3; and

when X is O and n is 1 R1 is H or an optionally substituted aliphatic group and R is an optionally substituted aromatic or aralkyl group provided that R is not of formula (b) where R15 is H, Cl, CH3, or CF3

ACTIVITY - Cytostatic; antiarthritic; antiarteriosclerotic; antipsoriatic; ophthalmological; antidiabetic; vulnerary; antiulcer; antibacterial; gynecological; antithyroid; cerebroprotective; antiallergic; antiinflammatory; hepatotropic; analgesic; antibacterial; immunosuppressive; virucide; fungicide; anti-HIV; protozoacide; dermatological; antisickling; osteopathic; keratolytic; vasotropic; cardiatic; antiviral; antiparasitic; antiprotozoal; antipyretic; circulatory active; antiasthmatic; respiratory active; antiinfertility.

MECHANISM OF ACTION - (I) are protein kinase inhibitors e.g. KDR/FLK-1/VEGFR-2 tyrosine kinase inhibitors and Flt-1/VEGFR-1 tyrosine kinase inhibitors and inhibitors of serine/threonine kinases e.g. CDKs, Plk-1 or Raf-1 and Src kinases e.g. Lck, Src, fyn, and yes.

USE - (I) are used to inhibit protein kinase and to treat hyperproliferative disorders, to affect angiogenesis, to treat cancer,

arthritis, atherosclerosis, psoriasis, hemangioma, myocardial angiogenesis, coronary and cerebral collateral vascularization, ischemic limb angiogenesis, corneal disease, rubeosis, neovascular glaucoma, macular degeneration, retinopathy of prematurity, wound healing, ulcers, Helicobacter-related diseases, fractures, endometriosis, diabetic retinopathy, cat scratch fever, thyroid hyperplasia, burns, trauma, acute lung injury, chronic lung disease, asthma, stroke, polyps, cysts, synovitis, chronic and allergic inflammation, ovarian hyperstimulation syndrome, pulmonary and cerebral edema, keloid, fibrosis, cirrhosis, carpal tunnel syndrome, sepsis, adult respiratory distress syndrome, multiple-organ dysfunction syndrome, ascites and tumor-associated effusions and edema, and to inhibit vascular hyperpermeability or the production of edema (claimed). They may be used to treat ulcers (bacterial, fungal and Mooren ulcers and ulcerative colitis), undesired angiogenesis, edema or stromal deposition occurring in viral infections such as herpes simplex, herpes zoster, AIDS, psoriasis, Kaposi's sarcoma, protozoan infections, toxoplasmosis, endometriosis, ovarian hyperstimulation syndrome, pre-eclampsia, menometrorrhagia, systemic lupus, sarcoidosis, synovitis, Crohn's disease, sickle cell anemia, Lyme's disease, pemphigoid, Paget's disease, hyperviscosity syndrome, ovarian stimulation syndrome, Osler-Weber-Rendu disease, arthritis, osteoarthritis, edema following trauma, radiation or stroke, ocular and macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser complications, conjunctivitis, anaphylaxis, Stargardt's disease, Eales disease, retinopathy, macular degeneration, cardiovascular conditions (atherosclerosis, restenosis, vascular occlusion, carotid obstructive disease, chronic occlusive pulmonary disease), cancer-related indications (solid tumors, sarcomas especially Ewing's sarcoma and osteosarcoma, retinoblastoma, rhabdomyosarcomas, neuroblastoma, hematopoietic malignancies including leukemia and lymphoma, tumor-induced pleural or pericardial effusions and malignant ascites), Crow-Fukase (POEMS) syndrome, and diabetic conditions such as glaucoma, diabetic retinopathy and microangiopathy. They also may be used to treat osteopetrosis, tumor-induced hypercalcemia and bone metastases.

ADVANTAGE - Due to the selectivity of (I) for specific kinases, there is a minimization of the side-effects that can occur when less selective kinase inhibitors are employed.

Dwg.0/0

L17 ANSWER 2 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2000-052651 [04] WPIDS

DOC. NO. CPI: C2000-013524

TITLE: New 3-(3-cyclopentyloxy-4-methoxyphenyl)-3-phenylcyanocyclobutan-1-one derivatives useful as phosphodiesterase isoenzyme denominated 4 inhibitors.

DERWENT CLASS: B05

INVENTOR(S): CHRISTENSEN, S B; FORSTER, C J

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 22

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9952848	A1	19991021	(200004)*	EN	34
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP US					
US 6118017	A	20000912	(200046)		

US 6172118 B1 20010109 (200104)
 EP 1071646 A1 20010131 (200108) EN
 R: BE CH DE ES FR GB IT LI NL
 JP 2002511439 W 20020416 (200242) 54

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9952848	A1	WO 1999-US8001	19990413
US 6118017	A Provisional	US 1998-81643P	19980414
		US 1999-291576	19990408
US 6172118	B1 Provisional	US 1998-81643P	19980414
		US 1999-291592	19990408
EP 1071646	A1	EP 1999-921382	19990413
		WO 1999-US8001	19990413
JP 2002511439 W		WO 1999-US8001	19990413
		JP 2000-543411	19990413

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1071646	A1 Based on	WO 9952848
JP 2002511439 W	Based on	WO 9952848

PRIORITY APPLN. INFO: US 1998-81643P 19980414; US 1999-291576
 19990408; US 1999-291592 19990408

AN 2000-052651 [04] WPIDS

AB WO 9952848 A UPAB: 20000124

NOVELTY - 3-(3-cyclopentyloxy-4-methoxyphenyl)-3-phenylcyanocyclobutan-1-one derivatives, useful as phosphodiesterase isoenzyme denominated 4 inhibitors, are new.

DETAILED DESCRIPTION - 3-(3-cyclopentyloxy-4-methoxyphenyl)-3-phenylcyanocyclobutan-1-one derivatives of formula (I) and their salts are new:

R1 = -(CR4R5)nC(O)O(CR4R5)mR6, -(CR4R5)nC(O)NR4(CR4R5)mR6, -(CR4R5)nCO(CR4R5)mR6 or -(CR4R5)rR6, where the alkyl may be substituted with one or more F;

m = 0-2;

n = 1-4;

r = 0-6;

R4, R5 = H or 1-2C alkyl;

R6 = H, methyl, OH, aryl, haloaryl, (halo)aryloxy-(1-3C)-alkyl, indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanlyl, (tetrahydro)pyranlyl, (tetrahydro)thienyl, (tetrahydro)thiopyranlyl, 3-6C cycloalkyl or 4-6C cycloalkyl with 1-2 unsaturated bonds where cycloalkyl or heterocyclic are optionally substituted with 1-3 methyl, ethyl or OH;

X = VR2, halo, nitro, NR4R5 or formyl amine;

V = O or S(O)m';

q, m' = 0-2;

X2 = O or NR8;

R2 = 1-2C alkyl optionally substituted with 1 or more F;

R3 = H, halo, or 1-4C alkyl optionally substituted by halo, CH2NHC(O)C(O)NH2, CH=CR8'R8', cyclopropyl optionally substituted by R8', CN, OR8, CH2OR8, NR8R10, CH2R8R10, C(=Z)H, C(=O)OR8, C(=O)NR8R10 or CCR8;

Z = O, NR9, NOR8, NCN, C(-CN)2, CR8CN, CR8NO2, C(-CN)C(=O)OR9 and C(-CN)C(=O)NR8R8;

A = O, NR7, NCR4R52-6C alkenyl, NOR14, NOR15, NOCR4R52-6 C alkenyl, NNR4R14, NNR4R15, NCN, NNR8C(O)NR8R14, NNR8R14, NNR8C(=S)NR8R14, 2(1,3-dithiane), 2(1,3-dioxiolane), 2(1,3-dioxane), 2(1,3-dioxathiolane), di(m)ethyl ketal or di(m)ethylthioketal;

R7 = -(CR4R5)qR12 or 1-6C alkyl where R12 or 1-6 alkyl are optionally substituted by 1-3 F, Br, Cl, nitro, NR10R11, C(O)R8, CO2R8, O(CH2)qR8, CN, C(O)NR10R11, O(CH2)qC(O)NR10R11, O(CH2)qC(O)R8, NR10C(O)NR10R11, NR10C(O)R11, NR10C(O)OR9, NR10C(O)OR13, C(NR10)NR10R11, C(NCN)NR10R11, C(NCN)SR9, NR10C(NCN)SR9, NR10C(NCN)NR10R11, NR10S(O)2R9, S(O)mR9, NR10C(O)C(O)NR10R11, NR10C(O)C(O)R10 or R13;

R12 = R13, 3-7C cycloalkyl, (2-, 3-, or 4-pyridyl), pyrimidyl, pyrazolyl, (1-or 2-imidazolyl), pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, (2-, or 3-thienyl), quinolyl, naphthyl or phenyl;
R8 = H or R9;

R8' = F or R8;

R9 = 1-4C alkyl optionally substituted with 1-3F;

R10 = OR8 or R11;

R11 = H or R9; or

NR10R11 = 5-7 membered ring with at least 1 heteroatom from O, N or S;

R13 = oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl or thiadiazolyl connected through a carbon atom optionally substituted with one or two 1-2C alkyl; and

R14 = H or R7; when R8 and R14 = NR8R14 they form a 5-7 membered ring with at least 1 heteroatom from O, N or sulfur (S) provided that:

R15 = C(O)R14, C(O)R4R14, S(O)2R7 or S(O)2NR4R14:

provided that when R6 = OH, m = 2 and r = 2-6, and when R6 = 2-tetrahydro-pyranyl, -thiopyranyl, -furanyl, or -thienyl, m = 1-2 and r = 1-6, and when n = 1 and m = 0, then R6 is not H in - (CR4R5)nCO(CR4R5)mR6.

INDEPENDENT CLAIMS are also included for the following:

(1) a compound of formula (II) and its salts;

(2) compositions comprising (I) and an excipient; and

(3) compositions comprising (II) and an excipient:

B' = OR14, OR15, SR14, S(O)mR7, S(O)2NR10R14, NR10R14, NR14C(O)R9, NR10C(=Y')R14, NR10C(O)OR7, NR10C(=Y')NR10R14, NR10S(O)2NR10R14, NR10C(NCN)NR10R14, NR10S(O)2R7, NR10C(CR4NO2)NR10R14, NR10C(=N-CN)SR9, NR10C(CR4NO2)SR9, NR10C(NR10)NR10R14, NR10C(O)C(O)NR10R14, C(=Y')R14, C(O)OR14, C(=Y')R14, COOR14, C(=Y')NR10R14, C(NR10)NR10R14, CN, C(=N-OR8)R14, C(=NOR14)R8, C(NR8)NR10R14, C(NR14)NR8R8', C(=N-CN)NR10R14, C(=N-CN)SR11, (2-, 4-, or 5-imidazolyl), (3-, 4- or 5-pyrazolyl), (4- or 5-triazolyl(1,2,3)), (3- or 5-triazolyl(1,2,4)), 5-tetrazolyl, (2-, 4-, or 5-oxazolyl), (3- or 5-oxadiazolyl(1,2,4)), (2-oxadiazolyl(1,3,4)), (2-thiadiazolyl(1,3,4)), (2-, 4- or 5-thiazolyl), (2-, 4-, or 5-oxazolidinyl), (2-, 4-, or 5-thiadiazolinyl) or (2-, 4-, or 5-imidazolidinyl) where all heterocyclic rings are optionally substituted with 1 or more R14; and
Y' = O or S;

provided that when R12 is N-pyrazolyl, N-imidazolyl, N-triazolyl, N-pyrrolyl, N-piperazinyl or N-morpholinyl, then q is not 1.

ACTIVITY - Antiasthmatic; airway smooth muscle relaxant; mast cell mediator release inhibitor; neutrophil degranulation suppressant; basophil degranulation inhibitor; monocyte activation inhibitor; macrophage activation inhibitor; fungicide; antiyeast; antiyeast toxicity reducer; fungicide toxicity reducer; virucide.

MECHANISM OF ACTION - Phosphodiesterase isoenzyme denominated 4 (PDE 4) inhibitor. Tumor Necrosis Factor (TNF) inhibitor.

USE - Used for treating asthma or chronic obstructive pulmonary disease in humans (claimed). Also useful for treating:

(1) allergic and inflammatory diseases e.g. dermatitis, psoriasis, septic shock, Crohn's disease, rheumatoid arthritis and reperfusion injury;

(2) viral infections giving elevated TNF release e.g. human immune deficiency virus (HIV), influenza, adenoviruses, herpes, retroviruses and veterinary viruses; and

(3) yeast or fungal infections giving elevated TNF release e.g. fungal meningitis.

The compounds are also useful for reducing the toxicity of antifungals, antibacterials and antivirals e.g. amphotericin B.

ADVANTAGE - The pharmacological action is potentiated by the presence of autocoids and hormones that are released during extrinsic asthmatic attacks.

Dwg.0/0

L17 ANSWER 3 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1997-362977 [33] WPIDS

CROSS REFERENCE: 1995-036375 [05]; 1998-167941 [15]; 2000-205222 [18]; 2002-711569 [77]

DOC. NO. CPI: C1997-116310

TITLE: Treatment of bacterial and parasitic infections - comprises administration of lavendamycin analogue.

DERWENT CLASS: B02

INVENTOR(S): BEHFOROUZ, M; MERRIMAN, R L

PATENT ASSIGNEE(S): (UYBA-N) UNIV BALL STATE

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5646150	A	19970708	(199733)*		31

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5646150	A	CIP of	US 1993-71648 19930604
			US 1994-345509 19941128

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5646150	A	CIP of US 5525611

PRIORITY APPLN. INFO: US 1994-345509 19941128; US 1993-71648 19930604

AN 1997-362977 [33] WPIDS

CR 1995-036375 [05]; 1998-167941 [15]; 2000-205222 [18]; 2002-711569 [77]

AB US 5646150 A UPAB: 20021204

Treatment of a bacterial or parasitic infection comprises administration of a lavendamycin analogue of formula (I). X = NHC(=O)R10 or NHC(=S)R10; Y = H; OR11, SR11, N(R11)2, NR11N(R11)2, halo, NO2, CN, C(=NR11)R11, C(=O)R12, C(=S)R12 or C(=S)R13; 1-20C alkyl, aryl, 3-8C cycloalkyl, 2-20C alkynyl, 2-20C alkenyl, thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl,

isoxazolyl, thiazolyl, **oxadiazolyl** or thiadiazolyl (all optionally substituted by one Rx, NH₂, RxNH, (Rx)₂N, CN, N₃, NO₂, OH, halo, SH, RxS, RxSO₂, RxSO, RxO, COOH, COORx, CORx, CHO or CON(Rx)₂); R₄, R₆ = H halo, NO₂, CN, OR₁₃, SR₁₃, N(R₁₃)₂, C(=O)N(R₁₃)₂, C(=S)N(R₁₃)₂, C(=O)R₁₃, C(=S)R₁₃ or C(=NR₁₃)R₁₃; 1-20C alkyl optionally containing a heteroatom selected from O, S or N, aryl, 3-8C cycloalkyl, 2-20C alkenyl, 2-20C alkynyl, thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl** or thiadiazolyl (all optionally substituted by one Rx, NH₂, RxNH, (Rx)₂N, CN, N₃, NO₂, OH, halo, SH, RxS, RxSO₂, RxSO, RxO, COOH, COORx, CORx, CHO or CON(Rx)₂); R₁₀, R₁₁, R₁₃ = H; 1-20C alkyl, 3-8C cycloalkyl, 2-20C alkenyl, 2-20C alkynyl, aryl, thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl** or thiadiazolyl (all optionally substituted by one Rx, NH₂, RxNH, (Rx)₂N, CN, N₃, NO₂, OH, halo, SH, RxS, RxSO₂, RxSO, RxO, COOH, COORx, CORx, CHO or CON(Rx)₂); R₁₂ = H, N(R₁₁)₂, OR₁₁, SR₁₁, NR₁₁N(R₁₁)₂, OR₁₄N(R₁₁)₂ or 1-20C alkyl, 3-8C cycloalkyl, aryl, 2-20C alkenyl, 2-20C alkynyl, thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl** or thiadiazolyl (all optionally substituted by one Rx, NH₂, RxNH, (Rx)₂N, CN, N₃, NO₂, OH, halogen, SH, RxS, RxSO₂, RxSO, RxO, COOH, COORx, CORx, CHO or CON(Rx)₂); R₁₄ = 1-20C alkylene; Rx = 1-20C alkyl, 3-8C cycloalkyl, aryl, 2-20C alkenyl, 2-20C alkynyl, thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl** or thiadiazolyl.

USE - (I) inhibit the growth of bacteria and parasites and are particularly useful against parasitic infections caused by Leishmania spp. (I) also have antitumour and antiviral effects. (I) are useful for treating both gram positive and gram negative bacteria e.g. bacteria of the genus Staphylococcus, Streptococcus. Viral infections which can be treated using (I) include Retroviridae such as HIV-1, and HIV-2, Herpesviridae such as **herpes** simplex and Epstein-Barr virus, Hepnaviridae such as hepatitis B and Picornaviridae. Parasitic infections also include those of Amoeba, Giardia, Babesia, Balantidium, Eimeriorina, Entamoeba, Histomonas, and Trypanosomatidae. (I) are especially effective against solid tumours and malignant tumours.
Dwg.2/2

L17 ANSWER 4 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1997-131824 [12] WPIDS

CROSS REFERENCE: 1993-336568 [42]

DOC. NO. CPI: C1997-042531

TITLE: New 1-phenyl-1-vinyl-cyclohexane derivs. - used as phosphodiesterase IV and TNF prodn. inhibitors, e.g. for treating inflammatory and allergic disease or fungal or viral infections.

DERWENT CLASS: B03 B05

INVENTOR(S): CHRISTENSEN, S B

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5602157	A	19970211	(199712)*		17

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5602157	A	CIP of	US 1992-862030
		CIP of	US 1992-968762
		CIP of	WO 1993-US1991
			US 1995-443641
			19920402
			19921030
			19930305
			19950518

PRIORITY APPLN. INFO: US 1995-443641 19950518; US 1992-862030
 19920402; US 1992-968762 19921030; WO
 1993-US1991 19930305

AN 1997-131824 [12] WPIDS

CR 1993-336568 [42]

AB US 5602157 A UPAB: 19970320

4-Substd. 1-(3,4-disubstd. phenyl)-1-vinylcyclohexane derivs. of formula (I) and their salts are new. X5 is absent if the optional bond is present; R1 = -(CR4R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6 (in which all alkyl moieties are opt. substd. by one or more halogens); m = 0-2; n = 1-4; r = 0-6; R4, R5 = H, Me or Et; R6 = H, Me, OH, opt. halo-substd. aryl, opt. halo-substd. aryloxy(1-3C)alkyl, indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, pyranal, tetrahydrothienyl, thienyl, thienyl, tetrahydrothiopyranal, thiopyranal, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds (where cycloalkyl and heterocyclic moieties are opt. substd. by 1-3 Me or one Et); X = YR2, halo, NO2, NR4R5 or HCONH; Y = O, S, SO or SO2; X2 = O or NR8; X3 = H or X; X5 = H, R9, OR8, CN, COR8, COOR8, CON(R8)2 or N(R8)2; R2 = 1-2C alkyl (opt. substd. by at least 1 halogen); s = 0-4; Z = C(Y')R14, COOR14, C(Y')NR10R14, C(NR10)NR10R14, CN, C(NOR8)R14, CONR8NR8COR8, CONR8NR10R14, C(NOR14)R8, C(NR8)NR10R14, C(NR14)N(R8)2, C(NCN)NR10R14, C(NCN)SR9, 2-, 4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl(1,2,3), 3- or 5-triazolyl(1,2,4), 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-oxadiazolyl(1,2,4), 2-oxadiazolyl(1,3,4), 2-thiadiazolyl(1,3,4), 2-, 4- or 5-thiazolyl, 2-, 4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl (where all heterocycles are opt. substd. by at least 1 gps. R14); Y' = O or S; R7 = -(CR4R5)qR12 or 1-6C alkyl (where R12 or the 1-6C alkyl gp. is opt. substd. by one or more 1-2C alkyl, itself opt. substd. by 1-3 F); or F, Cl, Br, NO2, NR10R11, COR8, COOR8, OR8, CN, CONR10R11, OCONR10R11, OCOR8, NR10CONR10R11, NR10COR11, NR10COOR9, NR10COR13, C(NR10)NR10R11, C(NCN)NR10R11, C(NCN)SR9, NR10C(NCN)SR9, NR10C(NCN)NR10R11, NR10SO2R9, SR9, SOR9, SO2R9, NR10COCONR10R11, NR10COCOR10, thiazolyl, imidazolyl, oxazolyl, pyrazolyl, triazolyl or tetrazolyl; q = 0-2; R12 = 3-7C cycloalkyl, 2-, 3- or 4-pyridyl, pyrimidyl, pyrazolyl, 1- or 2-imidazolyl, thiazolyl, triazolyl, pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, 2- or 3-thienyl, 4- or 5-thiazolyl, quinolinyl, naphthyl or phenyl; R8 = H or as R9; R81 = R8 or F; R9 = 1-4C alkyl (opt. substd. by 1-3 F); R10 = OR8 or R11; R11 = H or 1-4C alkyl (opt. substd. by 1-3 F); or NR10R11 = 5-7 membered ring opt. contg. at least one additional O, N or S heteroatom; R13 = oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, oxadiazolyl or thiadiazolyl (all bonded via C and opt. substd. by 1 or 2 1-2C alkyl); R14 = H or as R7; or NR10R14 may form a ring as for NR10R11; provided that (i) if R6 = OH, then m = 2 or r = 2-6, (ii) if R6 = 2-tetrahydropyranyl, 2-tetrahydrothiopyranal, 2-tetrahydrofuranyl or 2-tetrahydrothienyl, then m = 1 or 2 or r = 1-6,

(iii) if $n = 1$ and $m = 0$, then R6 is other than H in $-(CR4R5)nO(CR4R5)mR6$ and (iv) if R12 = pyrazolyl, imidazolyl, triazolyl, pyrrolyl, piperazinyl, piperidinyl or morpholinyl (all bonded via N), then q is not 1.

USE - (I) are tumour necrosis factor (TNF) prodn. inhibitors and phosphodiesterase IV (PDE IV) inhibitors, and are used for treating or preventing disorders mediated by TNF or PDE IV. As TNF prodn. inhibitors, (I) are useful for treating viral infections (e.g. infections by cytomegalovirus, adenovirus, influenza virus, **herpes** simplex, **herpes** zoster, veterinary viruses and esp. HIV), treating yeast and fungal infections (esp. fungal meningitis and Candida infections), reducing the toxicity of antifungal, antibacterial or antiviral agents (esp. the antifungal agent amphotericin B) and treating rheumatoid arthritis or spondylitis, osteoarthritis, gouty arthritis, sepsis, septic or endotoxic shock, Gram negative sepsis, toxic shock syndrome, ARDS, cerebral malaria, chronic pulmonary respiratory distress syndrome, silicosis, pulmonary sarcoidosis, bone resorption diseases, reperfusion injury, graft-versus-host reaction, allograft rejection, fever and myalgia due to infection (e.g. influenza), cachexia secondary to infection, malignancy or AIDS, ARC, AIDS, keloid or scar tissue formation, Crohn's disease, ulcerative colitis, pyresis and autoimmune diseases (e.g. multiple sclerosis, autoimmune diabetes or systemic lupus erythematosus). As PDE IV inhibitors (I) are useful for treating allergic and inflammatory diseases such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic or vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock and ARDS; and for treating diabetes insipidus and CNS disorders (e.g. depression and multi-infarct dementia). A method for treating an allergic or inflammatory disease using (I) is claimed.

Dwg.0/0

L17 ANSWER 5 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-321768 [32] WPIDS

DOC. NO. CPI: C1996-102463

TITLE: New 1,4-disubstd. 4-phenyl-cyclohexene derivs. - used as TNF prodn. and phosphodiesterase inhibitors, e.g. for treating allergy, inflammation or viral or fungal infections.

DERWENT CLASS: B05 C02 C03

INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D; RYAN, M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9620175	A1	19960704	(199632)*	EN	31
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 799205	A1	19971008	(199745)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10513153	W	19981215	(199909)		43
EP 799205	B1	19990908	(199941)	EN	
R: BE CH DE DK FR GB IT LI NL					
DE 69512086	E	19991014	(199949)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9620175	A1	WO 1995-US16694	19951221
EP 799205	A1	EP 1995-944511	19951221
		WO 1995-US16694	19951221
JP 10513153	W	WO 1995-US16694	19951221
		JP 1996-520522	19951221
EP 799205	B1	EP 1995-944511	19951221
		WO 1995-US16694	19951221
DE 69512086	E	DE 1995-612086	19951221
		EP 1995-944511	19951221
		WO 1995-US16694	19951221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 799205	A1 Based on	WO 9620175
JP 10513153	W Based on	WO 9620175
EP 799205	B1 Based on	WO 9620175
DE 69512086	E Based on	EP 799205
	Based on	WO 9620175

PRIORITY APPLN. INFO: US 1994-363168 19941223

AN 1996-321768 [32] WPIDS

AB WO 9620175 A UPAB: 19960819

4-(3,4-Disubstd. phenyl)- 1,4-disubstd. or 1,2,4-trisubstd. cyclohexene derivs. of formula (I) and their salts are new: Z1 = Z and Z2 = H, i.e. cpds. (I'); or Z1 = Z'' and Z2 = Z', i.e. cpds. (I''); R1 = -(CR4R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6; where the alkyl moieties are opt. substd. by halogen(s); m = 0-2; n = 0-4; r = 0-6; R4, R5 = H, Me or Et; R6 = H, Me, OH, opt. halo substd. aryl, opt. halo substd. aryloxy(1-3C)alkyl, indanyl, indenyl, 7-11C polycycloalkyl, furanyl, pyranal, thienyl, thiopyranal (the last four opt. as tetrahydro derivs.), 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl or heterocyclic moieties are opt. substd. by 1-3 Me, one Et or one OH; provided that (a) if R6 = OH, then m = 2 or r = 2-6, (b) if R6 = 2-tetrahydro(pyranyl, thiopyranal, thienyl or furanyl), then m = 1 or 2 or r = 1-6 and (c) if m = 1 and n = 0, then R6 is other than H in -(CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or HCONH; Y = O or S(O)m'; m' = 0-2; X2 = O or NR8; X3 = H or X; R2 = methyl or ethyl, both opt. substd. by halogen(s); s = 0-4; W = 2-6C alkylene, 2-6C alkenylene or 2-6C alkynylene; R3 = substd. carboxy, carbamide or alkyl; Z = CN or opt. substd. thio, alcohol, ester carboxamide, 2-, 4- or 5-imidazolyl, pyrazolyl, 1,2,3-triazol-4- or 5-yl, 1,2,4-triazol-3- or 5-yl, 5-tetrazolyl, oxazolyl, isoxazolyl, 1,2,4- or 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, thiazolyl, 2-, 4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl; R8 = H or as R11; R11 = 1-4C alkyl (opt. substd. by 1-3 F).

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of

the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal, antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.
Dwg.0/0

L17 ANSWER 6 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321767 [32] WPIDS
 DOC. NO. CPI: C1996-102462
 TITLE: New 1,3-di substd. 1-phenyl-cyclohexane derivs. - used as TNF prodn. and phosphodiesterase inhibitors, e.g., for treating allergy, inflammation and viral or fungal infections.
 DERWENT CLASS: B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D; RYAN, M
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9620174	A1	19960704	(199632)*	EN	24
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 799204	A1	19971008	(199745)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511395	W	19981104	(199903)		33
US 5900417	A	19990504	(199925)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9620174	A1	WO 1995-US16709	19951221
EP 799204	A1	EP 1995-943941	19951221
		WO 1995-US16709	19951221
JP 10511395	W	WO 1995-US16709	19951221
		JP 1996-520527	19951221
US 5900417	A	WO 1995-US16709	19951221
		US 1996-596244	19960227

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 799204	A1 Based on	WO 9620174
JP 10511395	W Based on	WO 9620174
US 5900417	A Based on	WO 9620174

PRIORITY APPLN. INFO: US 1994-362727 19941223; US 1996-596244
 19960227
 AN 1996-321767 [32] WPIDS

AB WO 9620174 A UPAB: 19960819

1,3-Disubstd. or 1,3,3-trisubstd. 1-(3,4-disubstd. phenyl)- cyclohexane derivs. of formula (I) and their salts are new: R1 = - (CR5R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6, where alkyl moieties are opt. substd. by one or more F; m = 0-2; n = 0-4; r = 0-6; R4, R5 = H, Me or Et; R6 = H, Me, OH, opt. halo-substd. aryl, opt. substd. aryloxy-(1-3C)-alkyl, indanyl, indenyl, 7-11C polycycloalkyl, furanyl, pyranlyl, thienyl, thiopyranlyl (the last four opt. as tetrahydro derivs.), 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl and heterocyclic moieties are opt. substd. by 1-3 Me, one Et or one OH; provided that (a) if R6 = OH, then m = 2 or r = 2-6, (b) if R6 = 2-tetrahydro(pyranyl, thiopyranlyl, furanyl or thienyl), then m = 1 or 2 or r = 1-6 or (c) if n = 1 and m = 0, then R6 is other than H in -(CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or HCONH; Y = O or S(O)m'; m' = 0-2; X2 = O or NR8; X3 = H or X; R2 = methyl or ethyl, both opt. substd. by one or more F; R3 = COOR14, CONR4R14 or R7; W = 2-6C alkylene, 2-6C alkenylene or 2-6C alkynylene; s = 0-4; Z = -C(R8)2-Z'; R8 = H or R9; R9 = 1-4C alkyl (opt. substd. by 1-3 F); R7 = substd. alkyl; Z' = e.g. CN, tetrazolyl, imidazolyl, imidazoliny, pyrazolyl, thiazolyl, oxazolyl, oxazolidinyl, triazolyl, isoxazolyl, **oxadiazolyl**, thiadiazolyl, morpholinyl, piperidinyl, piperazinyl, pyrrolyl, or opt. substd. hydroxy, thio, sulphinyl, sulphonyl, amino or carboxy.

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal, antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.
Dwg.0/0

L17 ANSWER 7 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-321758 [32] WPIDS

DOC. NO. CPI: C1996-102453

TITLE: New bis-phenyl cyclohexenyl-aliphatic hydrocarbon derivs.
- used as TNF prodn. and phosphodiesterase inhibitors,
e.g. for treating allergy, inflammation or viral or
fungal infections.

DERWENT CLASS: B05 C02 C03

INVENTOR(S): CHRISTENSEN, S B; KARPINSKI, J M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 9620162	A1	19960704	(199632)*	EN	26
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RW:	AT	BE	CH	DE	DK	ES	FR	GB	GR	IE	IT	LU	MC	NL	PT	SE
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W: JP US
 EP 799186 A1 19971008 (199745) EN
 R: BE CH DE DK FR GB IT LI NL
 US 5777160 A 19980707 (199834)
 JP 10511390 W 19981104 (199903) 36

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9620162	A1	WO 1995-US13322	19951010
EP 799186	A1	EP 1995-938261	19951010
		WO 1995-US13322	19951010
US 5777160	A Cont of	US 1994-363179	19941223
		WO 1995-US13322	19951010
		US 1997-860295	19970623
JP 10511390	W	WO 1995-US13322	19951010
		JP 1996-520433	19951010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 799186	A1 Based on	WO 9620162
US 5777160	A Based on	WO 9620162
JP 10511390	W Based on	WO 9620162

PRIORITY APPLN. INFO: US 1994-363179 19941223; US 1997-860295
 19970623

AN 1996-321758 [32] WPIDS

AB WO 9620162 A UPAB: 19960819

Bis-(1-phenyl-4-substd. or 3,4-disubstd. cyclohex-3-enyl)-alkane, alkene or alkyne derivs. of formula (I) and their salts are new. Z1 = Z and Z2 = H, i.e. cpds. (I'); or Z1 = Z'' and Z2 = Z', i.e. cpds. (I''); R1 = -(CCR4R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR65, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6, where alkyl moieties are opt. substd. by halogen(s); R4, R5 = H, Me or Et; m = 0-2; n = 1-4; r = 0-6; R6 = H, Me, OH, opt. halo-substd. aryl, opt. halo substd. aryloxy-(1-3C)alkyl, indanyl, indenyl, 7-11C polycycloalkyl, furanyl pyranlyl, thienyl, thiopyranlyl (the last four opt. ashtetrahydro derivs.), 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl and heterocyclic moieties are opt. substd. by 1-3 Me, one Et or one OH; provided that (a) if R6 = OH, then m = 2 or r = 2-6, (b) if R6 = 2-tetrahydro(pyranyl, thiopyranlyl, furanyl or thienyl), then m = 1 or 2 or r = 1-6 and (c) if n = 1 and m = 0, then R6 is other than H in -(CR4R5)nO(CR4R5)+mR+6; X = YR2, F, NR4R5 or NCONH; Y = O or S(O)m'; m' = 0-2; X2 = O or NR8; X3 = H or X; R2 = methyl or ethyl, both opt. substd. by halogen(s); s = 0-4; W = 2-6C alkylene, 2-6C alkenylene or 2-6C alkynylene; Z, Z'' = e.g S(O)m'R9, OSO2R9, OR9, O(CR4R5)nOR9 or N(R9)2; Z' = CN or opt. substd. thiol, alcohol, carbamido or 2-, 4- or 5-imidazolyl, pyrazolyl, 1,2,3-triazol-4- or 5-yl, 1,2,4-triazol-3- or 5-yl, 5-tetrazolyl, oxazolyl, isoxazolyl, 1,2,4- or 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, thiazolyl, 2-, 4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl, R8 = H or R11; R9 = 1-10C alkyl, 2-10C alkenyl, 3-7C cycloalkyl, 4-6C cycloalkenyl, aryl, aralkyl, heteroaryl or heteroaralkyl, all opt. substd. by one or more F; R11 = 1-4C alkyl (opt. substd. by 1-3 F).

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of

PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis; Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

Dwg.0/0

L17 ANSWER 8 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321755 [32] WPIDS
 CROSS REFERENCE: 1996-341947 [34]
 DOC. NO. CPI: C1996-102450
 TITLE: New 3,3-di substd. cyclohexan-1-ylidene acetate derivs. -
 for treating allergic and inflammatory diseases, also
 inhibitors of tumour necrosis factor prodn..
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 18
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9620159	A1	19960704	(199632)*	EN	25
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
JP 2002503200	W	20020129	(200211)		35

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9620159	A1	WO 1995-US16293	19951214
JP 2002503200	W	WO 1995-US16293	19951214
		JP 1996-520488	19951214

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 2002503200	W Based on	WO 9620159

PRIORITY APPLN. INFO: US 1994-363665 19941223

AN 1996-321755 [32] WPIDS

CR 1996-341947 [34]

AB WO 9620159 A UPAB: 20020215

Phenyl-cyclohexan-1-ylidene acetate derivs. of formula (I) and their salts are new. R1 = (CR4R5)nCOO(CR4R5)mR6, (CR4R5)nCONR4(CR4R5)mR6, (CR4R5)rR6 or (CR4R5)nO(CR4R5)mR6; in which alkyl may be substd. by 1 or more halo; m = 0-2; n = 0-4; r = 0-6; each R4 and R5 = H, Me or Et; R6 = H, Me, OH,

aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanlyl, (tetrahydro)pyranlyl, (tetrahydro)thienyl, (tetrahydro)thiopyranlyl, 3-6C cycloalkyl, or 4-6C cycloalkyl with 1 or 2 unsatd. bonds; cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me, one ET or OH; provided that (a) when R6 = OH, m = 2 or r = 2-6; (b) when R6 = 2-tetrahydro-pyranlyl, -thiopyranlyl, -furanlyl or -thienyl, m = 1 or 2, or r = 1-6; (c) when n = 1 and m = 0 then R6 is not H in (CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or formyl amine; Y = O or SOM'; m' = 0-2; X2 = O or NR8; X3 = H or X; X4 = H, R9, OR8, CN, COR8, COOR8, CONR8R8 or NR8R8; R2 = Me or Et, opt. substd. by 1 or more halo; s = 0-4; W = 2-6C alkyl, alkenyl or alkynyl; R3 = e.g. opt. substd. ester, amide, alkyl, oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, **oxadiazolyl** or thiadiazolyl; Z = e.g. opt. substd. ester, amide or cyanomethyl

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes simplex**, **herpes zoster** or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

Dwg.0/0

L17 ANSWER 9 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-321753 [32] WPIDS

DOC. NO. CPI: C1996-102448

TITLE: New bis-phenylcyclohexanol substd. alkane, alkene and alkyne derivs. - for treating allergic and inflammatory diseases, also inhibitors of tumour necrosis factor prodn..

DERWENT CLASS: B03 B05 C02 C03

INVENTOR(S): CHRISTENSEN, S B; KARPINSKI, J M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9620157	A1	19960704	(199632)*	EN	26
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 799182	A1	19971008	(199745)	EN	
R: BE CH DE DK FR GB IT LI NL					
US 5723681	A	19980303	(199816)		10
JP 10511391	W	19981104	(199903)		37

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9620157	A1	WO 1995-US13323	19951010
EP 799182	A1	EP 1995-936355	19951010
		WO 1995-US13323	19951010
US 5723681	A	WO 1995-US13323	19951010
		US 1997-860288	19970623
JP 10511391	W	WO 1995-US13323	19951010
		JP 1996-520434	19951010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 799182	A1 Based on	WO 9620157
US 5723681	A Based on	WO 9620157
JP 10511391	W Based on	WO 9620157

PRIORITY APPLN. INFO: US 1994-362708 19941223; US 1997-860288
19970623

AN 1996-321753 [32] WPIDS

AB WO 9620157 A UPAB: 19960819

Phenylcyclohexanol derivs. of formula (I) and their salts are new. R1 = (CR4R5)nCOO(CR4R5)mR6, (CR4R5)nCONR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6 or (CR4R5)rR6 in which alkyl gps. are opt. substd. by 1 or more F; m = 0-2; n = 1-4; r = 0-6; R4, R5 = H or (m)ethyl; R6 = H, Me, OH, aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, tetrahydro-furanyl, -pyranyl, -thienyl or -thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl with 1 or 2 unsatd. bonds; all cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me or by 1 Et or OH; provided that when R6 = OH, then m = 2 or r = 2-6; or when R6 = 2-tetrahydro-pyranyl, -thiopyranyl, -furanyl or -thienyl, then m = 1 or 2 or r = 1-6; or when n = 1 and m = 0, then R6 is not H in (CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or formyl amine; Y = O or SOM; m' = 0-2; W = 2-6C alkyl, alkenyl or alkynyl; each X2 = O or NR8; each X3 = H, or X; R2 = Me or Et, opt. substd. by 1 or more F; s = 0-4; R8 = H or R9; R9 = 1-4C alkyl opt substd. by 1-3 F; Z = e.g. opt. substd. ether, thiol, sulphinyl, sulphonyl, amino, oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinylisoxazolyl, **oxadiazolyl** or thiadiazolyl

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes simplex**, **herpes zoster** or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

Dwg.0/0

ABEQ US 5723681 A UPAB: 19980421

Phenylcyclohexanol derivs. of formula (I) and their salts are new. R1 = (CR4R5)nCOO(CR4R5)mR6, (CR4R5)nCONR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6 or (CR4R5)rR6 in which alkyl gps. are opt. substd. by 1 or more F; m = 0-2; n = 1-4; r = 0-6; R4, R5 = H or (m)ethyl; R6 = H, Me, OH, aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, tetrahydro-furanyl, -pyranyl, -thienyl or -thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl with 1 or 2 unsatd. bonds; all cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me or by 1 Et or OH; provided that when R6 = OH, then m = 2 or r = 2-6; or when R6 = 2-tetrahydro-pyranyl, -thiopyranyl, -furanyl or -thienyl, then m = 1 or 2 or r = 1-6; or when n = 1 and m = 0, then R6 is not H in (CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or formyl amine; Y = O or SOM; m' = 0-2; W = 2-6C alkyl, alkenyl or alkynyl; each X2 = O or NR8; each X3 = H, or X; R2 = Me or Et, opt. substd. by 1 or more F; s = 0-4; R8 = H or R9; R9 = 1-4C alkyl opt substd. by 1-3 F; Z = e.g. opt. substd. ether, thiol, sulphonyl, sulphonyl, amino, oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinylisoxazolyl, **oxadiazolyl** or thiadiazolyl

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.
Dwg.0/0

L17 ANSWER 10 OF 23 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1996-321634 [32] WPIDS
DOC. NO. CPI: C1996-102371
TITLE: New substd. phenyl-cyclohexene and cyclohexanone derivs - are useful in treatment of allergic disorders, inflammatory disorders, viral infections, fungal infections, etc.
DERWENT CLASS: B03 B05 C02 C03
INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D; RYAN, M D; RYAN, D M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 67
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619995	A1	19960704	(199632)*	EN	58
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KP KR KZ LK LR LT LV MD MG MN MX NO NZ PL PT RO RU SD SG SI SK TJ TM TT UA US UZ VN					

ZA 9510884 A 19960828 (199639) 57
 AU 9646883 A 19960719 (199647)
 NO 9702898 A 19970820 (199744)
 EP 800393 A1 19971015 (199746) EN
 R: BE CH DE DK FR GB IT LI NL
 FI 9702673 A 19970819 (199747)
 CZ 9701962 A3 19980114 (199810)
 BR 9510521 A 19980714 (199835)
 MX 9704733 A1 19971001 (199901)
 US 5861421 A 19990119 (199911)
 KR 98700861 A 19980430 (199914)
 NZ 301453 A 19990225 (199914)
 HU 78042 T 19990628 (199931)
 AU 708349 B 19990805 (199943)
 CN 1175211 A 19980304 (200208)
 JP 2002516601 W 20020604 (200239) 90

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619995	A1	WO 1995-US16858	19951221
ZA 9510884	A	ZA 1995-10884	19951221
AU 9646883	A	AU 1996-46883	19951221
NO 9702898	A	WO 1995-US16858	19951221
		NO 1997-2898	19970620
EP 800393	A1	EP 1995-944527	19951221
		WO 1995-US16858	19951221
FI 9702673	A	WO 1995-US16858	19951221
		FI 1997-2673	19970619
CZ 9701962	A3	WO 1995-US16858	19951221
		CZ 1997-1962	19951221
BR 9510521	A	BR 1995-10521	19951221
		WO 1995-US16858	19951221
MX 9704733	A1	MX 1997-4733	19970623
US 5861421	A	WO 1995-US16858	19951221
		US 1997-860404	19970623
KR 98700861	A	WO 1995-US16858	19951221
		KR 1997-704318	19970623
NZ 301453	A	NZ 1995-301453	19951221
		WO 1995-US16858	19951221
HU 78042	T	WO 1995-US16858	19951221
		HU 1998-2635	19951221
AU 708349	B	AU 1996-46883	19951221
CN 1175211	A	CN 1995-197681	19951221
JP 2002516601	W	WO 1995-US16858	19951221
		JP 1996-520574	19951221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9646883	A Based on	WO 9619995
EP 800393	A1 Based on	WO 9619995
CZ 9701962	A3 Based on	WO 9619995
BR 9510521	A Based on	WO 9619995
US 5861421	A Based on	WO 9619995
KR 98700861	A Based on	WO 9619995

NZ 301453	A	Based on	WO 9619995
HU 78042	T	Based on	WO 9619995
AU 708349	B	Previous Publ.	AU 9646883
		Based on	WO 9619995
JP 2002516601	W	Based on	WO 9619995

PRIORITY APPLN. INFO: US 1995-455796 19950531; US 1994-456234
 19941223; US 1994-363130 19941223; US
 1997-860404 19970623

AN 1996-321634 [32] WPIDS

AB WO 9619995 A UPAB: 19990412

phenyl-cyclohexane derivs. of formula (I) and (II), and salts of these are new: R1 = QnC(O)OQmR6, QnC(O)NR4QmR6, QnOQmR6 or QrR6, in which alkyl moieties are opt. substd. by one or more F; m = 0-2; n = 0-4; r = 0-6; Q = CR4R5; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, or aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo); indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanyl, (tetrahydro)pyranyl, (tetrahydro)thienyl, (tetrahydro)thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, the cycloalkyl and heterocyclic moieties being opt. substd. by 1-3 Me, one Et or one OH; X = YR2, F, NR4R5 or formyl amine; Y = O, S, SO or SO2; X2 = O or NR8; R2 = Me or Et (both opt. substd. by one or more halo); s = 0-4; W = 2-6C alkyl, 2-6C alkenyl or 2-6C alkynyl; R3 = opt. substd. carboxy, amido or alkyl; Z = e.g. O, imino, oximo NCN; 2-(1,3-dithiol)ane), 2-(2,3-diox(ol)ane), 2-(1,3-oxathiolane), di(m)ethylthio ketal or di(m)ethyl ketal, Z' = e.g. opt. substd. 2-, 4- or 5-9 imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl[1,2,3], 3- or 5-triazolyl[1,2,4], 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-oxadiazolyl[1,2,4], 2-oxadiazolyl[1,3,4], 2-thiadiazolyl[1,3,4], 2-, 4- or 5-thiazolyl, 2-, 4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl; R8 = H or R9; R9 = 1-4C alkyl (opt. substd. by 1-3F).

USE - (I) and (II) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes simplex**, **herpes zoster** or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) and (II) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

ADVANTAGE - No further details.

Dwg. 0/0

L17 ANSWER 11 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-321633 [32] WPIDS

DOC. NO. CPI: C1996-102370

TITLE: New 3-phenyl, 1,3-di substd. cyclohexane and cyclohexene cpds. - are useful in treatment of, e.g. asthma, ulcerative colitis, reperfusion injury, diabetes insipidus and viral infections.

DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M;
 RYAN, M D
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619994	A1	19960704	(199632)*	EN	24
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 796097	A1	19970924	(199743)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511397	W	19981104	(199903)		33
US 5869677	A	19990209	(199913)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619994	A1	WO 1995-US16839	19951221
EP 796097	A1	EP 1995-944220	19951221
		WO 1995-US16839	19951221
JP 10511397	W	WO 1995-US16839	19951221
		JP 1996-520565	19951221
US 5869677	A	WO 1995-US16839	19951221
		US 1996-605167	19960227

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 796097	A1 Based on	WO 9619994
JP 10511397	W Based on	WO 9619994
US 5869677	A Based on	WO 9619994

PRIORITY APPLN. INFO: US 1994-363664 19941223; US 1996-605167
 19960227

AN 1996-321633 [32] WPIDS

AB WO 9619994 A UPAB: 19960819

Phenyl-cyclohexane derivs. of formulae (Ia), (Ib) and (Ic) and salts of these, are new: (Ia); (Ib); (Ic); R1 = QnC(O)O1QmR6, QnC(O)NR4QmR6, QnOQmR6 OR QrR6, in which alkyl moieties are opt. substd. by one or more halo; m = 0-2; n = 0-4; r = 0-6; Q = CR4R5; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH or aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo); indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanyl, (tetrahydro)pyranyl, (tetrahydro)thienyl, (tetrahydro)thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, the cycloalkyl and heterocyclic moieties being opt. substd. by 1-3 Me, one Et or one OH; X = YR2, F, NR4R5 or formyl amine; Y = O, SO or SO2; X2 = O or NR8; X3 = H or X; X4 = H, R9, OR8, CN, COR8, COOR8, CONR8R8 or NR8R8; R2 = Me or Et (both opt. substd. by one or more halo; s = 0-4; W = 2-6C alkyl, 2-6C alkenyl or 2-6C alkynyl; R3 = e.g. substd. carboxy, amino or alkyl; Z = e.g. CN, or opt. substd. alcohol, thiol, ester, 2-, 4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl[1,2,3], 3- or 5-triazolyl[1,2,4], 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-oxadiazolyl[1,2,4], 2-oxadiazolyl[1,3,4],

2-thiadiazolyl[1,3,4], 2-,4- or 5-thiazolyl, 2-,4- or 5-oxazolidinyl, 2-,4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl.

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases (claimed) including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivities, vernal conjunctivities, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal, antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

ADVANTAGE - No further details.

Dwg.0/0

L17 ANSWER 12 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321632 [32] WPIDS
 DOC. NO. CPI: C1996-102369
 TITLE: New 1,3,3-tri subst. cyclohexene-1 cpds. - are useful in treatment of, e.g. asthma, Crohn's disease, reperfusion injury, diabetes insipidus, fungal meningitis and viral infections.
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619993	A1	19960704	(199632)*	EN	32
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
US 5646158	A	19970708	(199733)		13
EP 801567	A1	19971022	(199747)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511660	W	19981110	(199904)		42

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619993	A1	WO 1995-US16713	19951221
US 5646158	A	WO 1995-US16713	19951221
		US 1996-605178	19960227
EP 801567	A1	EP 1995-943944	19951221
		WO 1995-US16713	19951221
JP 10511660	W	WO 1995-US16713	19951221
		JP 1996-520531	19951221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5646158	A	Based on WO 9619993
EP 801567	A1	Based on WO 9619993
JP 10511660	W	Based on WO 9619993

PRIORITY APPLN. INFO: US 1994-362728 19941223; US 1996-605178
19960227

AN 1996-321632 [32] WPIDS

AB WO 9619993 A UPAB: 19960819

phenyl-cyclohexene derivs. of formulae (Ia) and (Ib, and salts of these: (Ia); (Ib); R1 = QnC(O)OQmR6, QnC(O)NR4QmR6 or QrR6, in which alkyl moieties are opt. substd. by one or more halo; m = 0-2; n = 0-4; r = 0-6; Q = CR4R5; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, or aryl or aryloxy (1-3C)alkyl (both opt. substd. by halo); indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanyl, (tetrahydropyranyl, (tetrahydro)thienyl, (tetrahydro)thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, the cycloalkyl and heterocyclic moieties being opt. substd. by 1-3 Me, one Et or one OH; X = YR2, F, NR4R5 or formyl amine; Y = O, S, SO or SO2; X2 = O or NR8; X3 = H or X; R2 = Me or Et (both opt. substd. by one or more halo); s = 0-4; W = 2-6C alkyl, 2-6C alkenyl or 2-6C alkynyl; R3 = COOR14, CONR4R14 or R15; Z = e.g. opt. substd amino, thio, sulphinyl orsulphonyl, amido, or ester; Z'=e.g. CN or opt. substd. ester or amide 2-, 4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl[1,2,3], 3- or 5-triazolyl[1,2,4], 5-tetrazolyl, 2-,4- or 5-oxazolyl, 3- 4- or 5-isoxazolyl, 3- or 5-oxadiazolyl[1,2,4], 2-oxadiazolyl[1,3,4], 2-thiadiazolyl[1,3,4], 2-,4- or 5-thiazolyl, 2-,4- or 5-oxazolidinyl, 2-,4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes simplex**, **herpes zoster** or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

ADVANTAGE - No further details.

Dwg.0/0

ABEQ US 5646158 A UPAB: 19970813

A compound of Formula (Ia) or (Ib) wherein:

R1 is -(CR4R5)nC(O)O(CR4R5)mR6, -(CR4R5)nC(O)NR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6, or -(CR4R5)rR6 wherein the alkyl moieties are unsubstituted or substituted with one or more halogens; m is 0 to 2; n is 0 to 4; r is 0 to 6;

R4 and R5 are independently hydrogen or a C1-2 alkyl;

R6 is hydrogen, methyl, hydroxyl, aryl, halo substituted aryl, aryloxyC1-3 alkyl, halo substituted aryloxyC1-3 alkyl, indanyl, indenyl, C7-11 polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, pyranyl, tetrahydrothienyl, thienyl, tetrahydrothiopyranyl, thiopyranyl,

C3-6 cycloalkyl, or a C4-6 cycloalkyl containing one or two unsaturated bonds, wherein the cycloalkyl or heterocyclic moiety is optionally substituted by 1 to 3 methyl groups, one ethyl group or an hydroxyl group; provided that:

a) when R6 is hydroxyl, then m is 2; or

b) when R6 is hydroxyl, then r is 2 to 6; or

c) when R6 is 2-tetrahydropyranyl, 2-tetrahydrothiopyranyl, 2-tetrahydrofuranyl, or 2-tetrahydrothienyl, then m is 1 or 2; or d) when R6 is 2-tetrahydropyranyl, 2-tetrahydrothiopyranyl, 2-tetrahydrofuranyl, or 2-tetrahydrothienyl, then r is 1 to 6; e) when n is 1 and m is 0, then R6 is other than H in (CR4R5)nO(CR4R5)mR6; X is YR2, fluorine, NR4R5, or formyl amine; Y is O or S(O)m'; m' is 0, 1, or 2; X2 is O or NR8; X3 is hydrogen or X; R2 is -CH3 or -CH2CH3 unsubstituted or substituted by 1 or more halogens; s is 0 to 4;

W is alkyl of 2 to 6 carbons, alkenyl of 2 to 6 carbons or alkynyl of 2 to 6 carbons; R3 is COOR14, C(O)NR4R14 or R15;

Z is S(O)m R9, OS(O)2R9, OR9, OC(O)NR7R7, OC(O)(O)qR7, O(CR4R5)nOR9, or NR9R9; q is 0 or 1; R7 is hydrogen or R9;

R8 is hydrogen or C1-4 alkyl unsubstituted or substituted by one to three fluorines, or when R8 and R10 are as -NR8R10 they together with the nitrogen form a 5 to 7 membered ring comprised only of carbon atoms or carbon atoms and at least one heteroatom selected from O, N, or S; R9 is C1-10 alkyl, C2-10 alkenyl, C3-7cycloalkyl, C4-6 cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, each of which are optionally substituted by one or more fluorine atoms, or two R9 terms appearing as NR9R9 together with the nitrogen form a 5 to 7 membered ring comprised only of carbon atoms or carbon atoms and at least one heteroatom selected from O, N, or S;

R10 is OR8 or R8; R11 is C1-4 alkyl unsubstituted or substituted by one to three fluorines; R12 is R13, C3-C7 cycloalkyl, or an unsubstituted or substituted aryl or heteroaryl group selected from the group consisting of (2-, 3- or 4-pyridyl), pyrimidyl, pyrazolyl, (1- or 2-imidazolyl), pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, (2- or 3-thienyl), quinolinyl, naphthyl, and phenyl;

R13 is a substituted or unsubstituted heteroaryl group selected from the group consisting of oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, **oxadiazolyl**, and thiadiazolyl, and where R13 is substituted on R12 or R13 the rings are connected through a carbon atom and each second R13 ring are optionally substituted by one or two C1-2 alkyl groups unsubstituted or substituted on the methyl with 1 to 3 fluoro atoms; R14 is hydrogen or R15; or when R10 and R14 are as NR10R14 they may together with the nitrogen form a 5 to 7 membered ring comprised only of carbon atoms or carbon atoms and at least one heteroatom selected from O, N, or S;

R15 is -(CR4R5)tR12 or C1-6 alkyl wherein the R12 or C1-6 alkyl group is unsubstituted or substituted by one or more times by methyl or ethyl unsubstituted or substituted by one to three fluorines, -F, -Br, -Cl, -NO2, -Si(R4)2, -NR8R10, -C(O)R8, -C(O)OR8, -O(CH2)qR8, -CN, -C(O)NR8R10, -O(CH2)qC(O)NR8R10, -O(CH2)qC(O)R10, -NR10C(O)NR8R10, -NR10C(O)R8, -NR10C(O)OR9, -NR10C(O)R13, -C(NR10)NR8R10, -C(NCN)NR8R10, -C(NCN)SR11, -NR10C(NCN)SR11, -NR10C(NCN)NR10R8, -NR10S(O)2R9, -S(O)m'R11, -NR10C(O)C(O)NR8R10, -NR10C(O)C(O)R10, or R13;

t is 0, 1, or 2; provided that:

f) when q is 1 in OC(O)(O)qR7, then R7 is not hydrogen;

g) R7 is not C1-4 alkyl unsubstituted or substituted by one to three fluorines; or the pharmaceutically acceptable salts thereof.

Dwg.0/0

L17 ANSWER 13 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321629 [32] WPIDS
 DOC. NO. CPI: C1996-102366
 TITLE: New phenyl-cyclohexane and phenyl-cyclohexene cpds - are useful as phosphodiesterase IV inhibitors and inhibitors of tumour necrosis factor prodn.
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M; RYAN, M D
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619990	A1	19960704	(199632)*	EN	31
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 796096	A1	19970924	(199743)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511398	W	19981104	(199903)		41
US 5863926	A	19990126	(199911)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619990	A1	WO 1995-US16857	19951221
EP 796096	A1	EP 1995-944526	19951221
		WO 1995-US16857	19951221
JP 10511398	W	WO 1995-US16857	19951221
		JP 1996-520573	19951221
US 5863926	A	WO 1995-US16857	19951221
		US 1997-860401	19971006

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 796096	A1 Based on	WO 9619990
JP 10511398	W Based on	WO 9619990
US 5863926	A Based on	WO 9619990

PRIORITY APPLN. INFO: US 1994-363123 19941223; US 1997-860401
 19971006

AN 1996-321629 [32] WPIDS

AB WO 9619990 A UPAB: 19960819

Phenyl-cyclohexane derivs. of formulae (Ia) and (Ib), and salts of these, are new: (Ia); (Ib); R1 = QnC(O)OQmR6, QnC(O)NR4QmR6, QnOQmR6 or QrR6, in which alkyl moieties are opt. substd. by one or more F; m = 0-2; n = 0-4; r = 0-6; Q = CR4R5; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, or aryl or aryloxy (1-3C) alkyl (both opt. substd. by halo); indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanyl, (tetrahydro)pyranyl, (tetrahydro)thienyl, (tetrahydro)thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, the cycloalkyl and heterocyclic moieties being opt. substd. by 1-3 Me, one Et or one OH; X = YR2 F, NR4R5 or formyl amine; Y = O, S, SO or SO2; X2 = O or NR8; X3 = H or X; X4 = H,

R9, OR8, CN, COR8, COOR8, CONR8R8 or NR8R8; R2 = Me or Et (both opt. substd. by one or more halo); R3 = COOR14, CONR4R14 or R7; s = 0-4; W = 2-6C alkyl, 2-6C alkenyl or 2-6C alkynyl; Z=e.g. opt. substd. thio, alcohol, ester carboxamide, 2-,4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl[1,2,3], 3- or 5-triazolyl[1,2,4], 5-tetrazolyl, 2-,4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-oxadiazolyl[1,2,4], 2-oxadiazolyl[1,3,4], 2-thiadiazolyl[1,3,4], 2-,4- or 5-thiazolyl, 2-,4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl; R8 = H or R9; R9 = 1-4C alkyl (opt. substd. by 1-3F);

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes simplex**, **herpes zoster** or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

ADVANTAGE - No further details.

Dwg. 0/0

L17 ANSWER 14 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321626 [32] WPIDS
 DOC. NO. CPI: C1996-102363
 TITLE: New 1,2 di substd. 4-phenyl-cyclohexane cpds - are useful as phosphodiesterase IV inhibitors and inhibitors of tumour necrosis factor prodn.
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; KARPINSKI, J M; RYAN, M D
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619986	A1	19960704	(199632)*	EN	23
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 794773	A1	19970917	(199742)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511659	W	19981110	(199904)		32
US 5990119	A	19991123	(200002)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619986	A1	WO 1995-US16712	19951221
EP 794773	A1	EP 1995-943943	19951221
		WO 1995-US16712	19951221
JP 10511659	W	WO 1995-US16712	19951221

US 5990119	A	JP 1996-520530	19951221
		WO 1995-US16712	19951221
		US 1997-605033	19970623

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 794773	A1 Based on	WO 9619986
JP 10511659	W Based on	WO 9619986
US 5990119	A Based on	WO 9619986

PRIORITY APPLN. INFO: US 1994-363668 19941223; US 1997-605033
19970623

AN 1996-321626 [32] WPIDS

AB WO 9619986 A UPAB: 19960819

Phenyl-cyclohexane derivs. of formula (I), and salts of (I), are new: (I); R1 = QnC(O)OQmR6, QnC(O)NR4QmR6, QnOQmR6 or Qrr6, in which alkyl moieties are opt. substd. by one or more F; m = 0-2; n = 0-4; r = 0-6; Q = CR4R5; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH or aryl or aryloxy (1-3C)alkyl (both opt. substd. by halo); indanyl, indenyl, 7-11C polycycloalkyl, (tetrahydro)furanyl, (tetrahydro)pyranyl, (tetrahydro)thienyl, (tetrahydro)thiopyranyl, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, the cycloalkyl and heterocyclic moieties being opt. substd. by 1-3 Me, one Et or one OH; W = 2-6C alkyl, 2-6C alkenyl or 2-6C alkynyl; X = YR2, halo, F, NR4R5 or formyl amine; Y = O, S, SO or SO2; X2 = O or NR8; X3 = H or X; R2 = Me or Et (both opt. substd. by one or more F); R3 = COOR14, CONR4R14 or R7; s = 0-4; Z = e.g. CR8R8V; V = CN, tetrazolyl, imidazolyl, imidazolidinyl, pyrazolyl, thiazolyl, thiazolidinyl, oxazolyl, oxazolidinyl, triazolyl, isoxazolyl, **oxadiazolyl**, thiadiazolyl, morpholinyl, piperidinyl, piperazinyl, pyrrolyl or opt. substd. hydroxy, thiol, sulphonyl, sulphonyl, or amino; R8 = H or R9; R9 = 1-4C alkyl (opt. substd. by 1-3F)

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE-IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.

ADVANTAGE - No further details.

Dwg. 0/0

L17 ANSWER 15 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-321620 [32] WPIDS

DOC. NO. CPI: C1996-102357

TITLE: New bis-1-phenyl cyclohexyl-aliphatic hydrocarbon derivs.
- used as TNF prodn. and phosphodiesterase inhibitors,
e.g. for treating allergy, inflammation and viral or

fungal infections.
 DERWENT CLASS: B05 C02 C03
 INVENTOR(S): CHRISTENSEN, S B; KARPINSKI, J M
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619980	A1	19960704	(199632)*	EN	31
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 796092	A1	19970924	(199743)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 10511657	W	19981110	(199904)		40

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619980	A1	WO 1995-US16708	19951221
EP 796092	A1	EP 1995-943940	19951221
		WO 1995-US16708	19951221
JP 10511657	W	WO 1995-US16708	19951221
		JP 1996-520526	19951221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 796092	A1 Based on	WO 9619980
JP 10511657	W Based on	WO 9619980

PRIORITY APPLN. INFO: US 1994-363166 19941223

AN 1996-321620 [32] WPIDS

AB WO 9619980 A UPAB: 19960819

Bis-(3-Oxo-1-phenylcyclohexyl)-alkane, alkene or alkyne derivs. and analogues of formula (I) and their salts are new. Z1 = Z and Z2 = H, i.e. cpds. (I'); or Z1 = 0 and Z2 = Z', i.e. cpds. (I''); R1 = -(CR4R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6, where alkyl moieties are opt. substd. by one or more F; m = 0-2; n = 0-4; r = 0-6; R4, R5 = H, Me or Et; R6 = H, Me, OH, opt. halo substd. aryl, opt. halo substd. aryloxy-(1-3C)alkyl, indanyl, indenyl, 7-11C polycycloalkyl, furanyl, pyranal, thienyl, thiopyranal (the last four opt. as tetrahydro derivs.), 3-6C cycloalkyl, 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl or heterocyclic moieties are opt. substd. by 1-3 Me, one Et or one OH; provided that (a) if R6 = OH, then m = 2 or r = 2-6, (b) if R6 = 2-tetrahydro(pyranyl, thiopyranal, furanyl or thienyl), then m = 1 or 2 or r = 1-6 or (c) if n = 1 and m = 0, then R6 is other than H in -(CR4R5)nO(CR4R5)mR6; W = 2-6C alkylene, 2-6C alkenylene or 2-6C alkynylene; X = YR2, F, NR4R5 or NCONH; Y = 0 or S(O)m'; m' = 0-2; X2 = 0 or NR8; X3 = H or X; R2 = methyl or ethyl (both opt. substd. by one or more F); s = 0-4; Z = e.g. O, imino, opt. substd. oxime, NCN, C(CN)OCOR9, C(CN)OR9, 2-(1,3-dithiane), 2-(1,3-dithiolane), dimethylthio ketal, diethylthio ketal, 2-(1,3-dioxolane), 2-(1,3-dioxan), 2-(1,3-oxathiolane), dimethyl ketal or diethyl ketal; Z' = e.g. opt. substd. alcohol, thio, amido, C(NCN)SR9, imidazol-2-, 4- or 5-yl, pyrazolyl, 1,2,3-triazol-4- or 5-yl, 1,2,4-triazol-3- or 5-yl, 5-tetrazolyl,

oxazolyl, isoxazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, thiazolyl, oxazolidin-2-,4- or 5-yl, thiazolidin-2-, 4- or 5-yl or imidazolidin-2-, 4- or 5-yl, R8 = H or R9; R9 = 1-4C alkyl (opt. substd. by 1-3 F)

USE - (I) inhibit phosphodiesterase IV (PDE IV) and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases (claimed) including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus), partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal, antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.
Dwg.0/0

L17 ANSWER 16 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1996-321618 [32] WPIDS
 DOC. NO. CPI: C1996-102355
 TITLE: New bis-1-phenyl cyclohexenyl-aliphatic hydrocarbon derivs. - used as TNF prodn. and phosphodiesterase inhibitors, e.g. for treating allergy, inflammation or viral or fungal infections.
 DERWENT CLASS: B05 C02 C03
 INVENTOR(S): CHRISTENSEN, S B; KARPINSKI, J M
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 19
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9619978	A1	19960704	(199632)*	EN	28
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 841908	A1	19980520	(199824)	EN	
R: BE CH DE DK FR GB IT LI NL					
US 5795918	A	19980818	(199840)		
JP 10511661	W	19981110	(199904)		37

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9619978	A1	WO 1995-US16714	19951221
EP 841908	A1	EP 1995-943945	19951221
		WO 1995-US16714	19951221
US 5795918	A	WO 1995-US16714	19951221
		US 1996-605182	19960227
JP 10511661	W	WO 1995-US16714	19951221
		JP 1996-520532	19951221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 841908	A1	Based on WO 9619978
US 5795918	A	Based on WO 9619978
JP 10511661	W	Based on WO 9619978

PRIORITY APPLN. INFO: US 1994-362709 19941223; US 1996-605182
19960227

AN 1996-321618 [32] WPIDS

AB WO 9619978 A UPAB: 19960819

Bis-(1-phenyl-3-substd. or 3,4-disubstd. cyclohex-2- or 3-enyl)alkane, alkene or alkyne derivs. of formula (I), and their salts are new. Z1 - Z, Z2 = H and a 3(4)-double bond is present, i.e. cpds. (I'); Z1 = Z, Z2 = H and a 2(3)-double bond is present, i.e. cpds. (I''); or Z1 = Z'', Z2 = Z' and a 3(4)-double bond is present, i.e. cpds. (I'''); R1 = -(CR4R5)nCOO(CR4R5)mR6, -(CR4R5)nCONR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6, where alkyl moieties are opt. substd. by halogen(s); m = 0-2; n = 0-4; r = 0-6; R4, R5 = H, Me or Et; R4, R5 = H, Me or Et; R6 = H, Me, OH, opt. halo substd. aryl, opt. halo substd. aryloxy-(1-3C)alkyl, indanyl, indenyl, 7-11C polycycloalkyl, furanyl, thienyl, pyranlyl, thiopyranlyl (the last four opt. as tetrahydro derivs.), 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl and heterocyclic moieties are opt. substd. by 1-3 Me, one Et one OH; provided that (a) if R6 = OH, then m = 2 or r = 2-6, (b) if R6 = 2-tetrahydro(pyranyl, thiopyranlyl, thienyl or furanyl, then m = 1 or 2 or r = 1-6 or (c) if n = 1 and m = 0, then R6 is other than H in (CR4R5)nO(CR4R5)mR6; X = YR2, F, NR4R5 or HCONH; Y = O or S(O)m; m' = 0-2; X2 = O or NR8; X3 = H or X; R2 = methyl or ethyl, both opt. substd. by halogen(s); s = 0-4; W = 2-6C alkylene, 2-6C alkenylene or 2-6C alkynylene; Z, Z'' = e.g. S(O)m, R9, OSO2R9, OR9 or opt. substd. amino; Z' = e.g. CN, or opt. substd. 2-, 4- or 5-imidazolyl, pyrazolyl, 1,2,3-triazol-4- or 5-yl, 1,2,4-triazol-3- or 5-yl, 5-tetrazolyl, oxazolyl, isoxazolyl, 1,2,4- or 1,3,4-oxadiazolyl, 1,3,4-thiadiazolyl, thiazolyl, 2-, 4- or 5-oxazolidinyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl, ester or carbamide.

USE - (I) inhibit phosphodiesterase IV (PDE) IV and prodn. of tumour necrosis factor (TNF). They are used for treatment or prophylaxis of PDE IV- or TNF-mediated diseases, specifically: (i) allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxin shock and ARDS; (ii) diabetes insipidus and CNS disorders such as depression and multiinfarct dementia; (iii) viral infections, esp. infections by HIV, cytomegalovirus, influenza virus, adenovirus, **herpes** simplex, **herpes** zoster or animal viruses (e.g. FIV, equine infectious anaemia, caprine arthritis, visna or maedi virus) partic. HIV; and (iv) yeast and fungal infections, esp. fungal meningitis. (I) are also useful for reducing the toxicity of antifungal, antibacterial or antiviral agents, specifically amphotericins, partic. amphotericin B.
Dwg. 0/0

L17 ANSWER 17 OF 23 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1995-373541 [48] WPIDS

DOC. NO. CPI: C1995-161823

TITLE: New substd. bi phenyl derivs. - are phosphodiesterase IV

and TNF inhibitors.
 DERWENT CLASS: B05
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 18
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9527692	A1	19951019	(199548)*	EN	4
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: JP US					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9527692	A1	WO 1995-US4294	19950407

PRIORITY APPLN. INFO: US 1994-225118 19940408

AN 1995-373541 [48] WPIDS

AB WO 9527692 A UPAB: 19951204

Substituted biphenyl derivs. of formula (I) and their salts are new. R1 = (CR4R5)nC(=O)O(CR4R5)mR6, (CR4R5)nC(=O)NR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6 or (CR4R5)rR6 (where each alkyl moiety is opt. substd. by halo); R2 = Me or Et (both opt. halogenated); R4, R5 = H, Me or Et; R6 = H, Me, OH, aryl, haloaryl, aryloxy-3-alkyl, (opt. halogenated); or indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, pyranal, tetrahydrothienyl, thienyl, tetrahydrothiopyranal, thiopyranal, 3-6C cycloalkyl or 4-6C cycloalkyl contg. 1-2 unsaturated bonds (all opt. substd. by 1-3 Me, 1 Et or 1 OH gp.); R7 = (CR4R5)qR12 or 1-6C alkyl where R12 or 1-6C alkyl are opt. substd. by 1-2C alkyl (opt. substd. by 1-3Q); Q = F, Br, Cl, NO2, NR10R11, C(=O)R8, C(=O)OR8, OR8, CN, C(=O)NR10R11, OC(=O)NR10R11, OC(=O)R8, NR10C(=O)NR10R11, NR10C(=O)R11, NR10C(=O)OR9, NR10C(=O)R13, C(=NR10)NR10R11, C(=N-CN)NR10R11, C(=N-CN)SR9, NR10C(=N-CN)NR10R11, NR10S(=O)2R9, -S(=O)mR9, NR10C(=O)C(=O)NR10R11, NR10C(=O)C(=O)R10 or R13; R8 = H or R9; R9, R11 = 1-4C alkyl (opt. substd. by 1-3 F); R10 = OR8 or R11; or NR10R11 = 5-7 membered ring contg. an additional O, N or S; R12 = 3-7C cycloalkyl, 2, 3 or 4-pyridyl, pyrimidyl, pyrazolyl, 1- or 2-imidazolyl, thiazolyl, triazolyl, pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, 2- or 3-thienyl, 4- or 5-thiazolyl, quinolinyl, naphthyl or phenyl; R13 = oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, **oxadiazolyl** or thiadiazolyl (all attached via C and opt. substd. by 1-2 of Me and/or Et); R14 = H or R7; or NR10R14 = 5-7 membered ring contg. at least one additional N, O or S; m, m' = 0-2; n = 1-4; r = 0-6; q = 0-2; X1 = YR6, halo, NO2, NR4R5 or formylamino; X2 = O or NR8; X3 = H or X1; Y = O or S(O)m'; Y' = O or S; Z, Z2, Z3 = H, (CH2)pCN, (CH2)pCO2R14, C(=O)H, C(=NR10)NR10R14, C(=NOR8)R14, C(=O)NR8NR8C(=O)R8, C(=O)NR8NR10R14, C(=NOR14)R8, C(=NR8)NR10R14, C(=NR14)NR8R8, C(=N-CN)NR10R14, C(=N-CN)SR9, 2, 4 or 5-imidazolyl, 3, 4 or 5-pyrazolyl, 4 or 5-triazolyl(1,2,3), 3 or 5-triazolyl(1,2,4), 5-tetrazolyl, 2, 4 or 5-oxazolyl, 3, 4 or 5-isoxazolyl, 3 or 5-**oxadiazolyl**(1,2,4), 2-**oxadiazolyl**(1,3,4), 2-thiadiazolyl(1,3,4), 5-thiadiazolyl(1,2,4), 2, 4 or 5-thiazolyl, 2, or 5-oxazolidinyl, 2, 4 or 5-thiazolidinyl, 2, 4 or 5-imidazolidinyl (all opt. substd. by R14); Z1 = H, OH, CN, CO2H, CO2Me or CONH2; p = 1-3; with

provisos. N.B. R2 and Y' do not appear in any formulae.

USE - (I) are TNF inhibitors and phosphodiesterase IV catalytic activity inhibitors used to treat allergic and inflammatory diseases including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock, ARDS, diabetes insipidus, CNS disorders such as depression and multi-infarct dementia, viruses, e.g. HIV-1, HIV-2, HIV-3, CMV, influenza, adenovirus and herpes viruses, e.g. Herpes zoster and Herpes simplex etc..

Dwg.0/0

L17 ANSWER 18 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1995-090571 [12] WPIDS
 DOC. NO. CPI: C1995-040944
 TITLE: New cyclohexyl or cyclohexenyl substd. phenyl cpds.
 inhibit TNF prodn and phosphodiesterase IV - used to
 treat e.g. inflammatory and allergic diseases, diabetes
 insipidus, CNS conditions, viral and fungal infections,
 etc..
 DERWENT CLASS: B03 B05
 INVENTOR(S): CHRISTENSEN, S B; FORSTER, C J
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 48
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9503794	A1	19950209	(199512)*	EN	40
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AU BB BG BR BY CA CN CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO					
RU SD SI SK UA US VN					
AU 9473751	A	19950228	(199522)		
ZA 9405643	A	19950426	(199523)		37
EP 714293	A1	19960605	(199627)	EN	
R: BE CH DE FR GB IT LI NL					
JP 09501420	W	19970210	(199716)		61
US 6300372	B1	20011009	(200162)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9503794	A1	WO 1994-US8581	19940729
AU 9473751	A	AU 1994-73751	19940729
ZA 9405643	A	ZA 1994-5643	19940729
EP 714293	A1	EP 1994-922761	19940729
		WO 1994-US8581	19940729
JP 09501420	W	WO 1994-US8581	19940729
		JP 1995-505999	19940729
US 6300372	B1	WO 1994-US8581	19940729
		US 1996-586770	19960130

FILING DETAILS:

PATENT NO	KIND	PATENT NO
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AU 9473751      A Based on      WO 9503794
EP 714293      A1 Based on      WO 9503794
JP 09501420    W Based on      WO 9503794
US 6300372    B1 Based on      WO 9503794

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PRIORITY APPLN. INFO: US 1993-130214 19931001; US 1993-99900
19930730; US 1996-586770 19960130

AN 1995-090571 [12] WPIDS

AB WO 9503794 A UPAB: 19950328

Cyclohexyl or cyclohexenyl substd. phenyl cpds. of formula (I) and their salts are new.

R1 = -(CR4R5)nC(O)O(CR4R5)mR6, -(CR4R5)nC(O)NR4(CR4R5)mR6,
-(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6 where the alkyl moieties are opt.
substd. by halo;

m = 0-2;

n = 1-4;

r = 0-6;

R4, R5 = H or 1-2C alkyl;

R6 = H, Me, OH, aryl opt. substd. by halo, aryloxy(1-3C)alkyl opt.
substd. by halo, indanyl, indenyl, 7-11C polycycloalkyl,
tetrahydrofuranyl, furanyl, tetrahydropyranyl, pyranal, tetrahydrothienyl,
thienyl, tetrahydrothiopyranal, thiopyranal, 3-6C cycloalkyl or 4-6C
cycloalkenyl contg. 1 or 2 unsatd. bonds, where the cycloalkyl or
heterocyclic gps. are opt. substd. by 1-3 Me or one Et;

provided that: (i) when R6 = OH, m = 2; or (ii) when R6 = OH, r =
2-6; or (iii) when R6 = 2-tetrahydropyranyl, 2-tetrahydrothiopyranal,
2-tetrahydrofuranyl or 2-tetrahydrothienyl, m = 1 or 2, or r = 1-6; (iv)
when n = 1 and m = 0, R6 is not H in -(CR4R5)nO(CR4R5)mR6;

X = YR2, halo, NO2, NR4R5 or formylamine;

Y = O or S(O)m';

m' = 0-2;

X2 = O or NR8;

X3 = H or X;

X4 = gp. (i) or (ii);

X5 = H, R9, OR8, CN, C(O)R8, C(O)OR8, C(O)N(R8)2 or N(R8)2;

R2 = CH3 or CH2CH3 opt. substd. by halo;

s = 0-4;

R3 = H, halo, 1-4C alkyl opt. substd. by halo, CH2NHC(O)C(O)NH2;

Z = CN, C(O)NR8NR8C(O)R8, C(NCN)SR9, 2-, 4- or 5-imidazolyl, 3-, 4-
or 5-pyrazolyl, 4- or 5-(1,2,3)triazolyl, 3- or 5-(1,2,4)triazolyl,
5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or
5-(1,2,4)oxadiazolyl, 2-(1,3,4)oxadiazolyl,
2-(1,3,4)thiadiazolyl, 2-, 4- or 5-thiazolyl, 2-, 4- or 5-oxazolidinyl,
2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl wherein all
heterocycles are opt. substd.;

R8 = H or R9;

R9 = 1-4C alkyl opt. substd. by 1-3 F.

USE - Cpds. (I) have tumour necrosis factor (TNF) and
phosphodiesterase IV (PDE IV) inhibitory activity. PDE IV inhibitors are
used to treat various allergic and inflammatory diseases, diabetes
insipidus and CNS disorders. (I) are also useful in treating viruses which
are sensitive to upregulation by TNF or will elicit TNF prodn. in vivo.
Such viruses include HIV-1, HIV-2, HIV-3, cytomegalovirus, influenza,
adenovirus and **Herpes** viruses. (I) may also be used to treat
viral infections in animals, and fungal and yeast infections affected by
TNF prodn. e.g., fungal meningitis. (I) may be co-administered with other
antifungal cpds.; and also used to reduce the toxicity of another

anti-fungal, anti-bacterial or anti-viral agents.
Dwg.0/0

L17 ANSWER 19 OF 23 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1995-036375 [05] WPIDS
CROSS REFERENCE: 1997-362977 [33]; 1998-167941 [15]; 2000-205222 [18];
2002-711569 [77]
DOC. NO. CPI: C1995-016309
TITLE: New antitumour, antiviral Lavendamycin analogues - active
against breast, colon tumours, parasitic infections,
retroviruses, etc..
DERWENT CLASS: B03 C02
INVENTOR(S): BEHFOROUZ, M; MERRIMAN, R L
PATENT ASSIGNEE(S): (BEHF-I) BEHFOROUZ M; (MERR-I) MERRIMAN R L
COUNTRY COUNT: 54
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9429308	A1	19941222	(199505)*	EN	103
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ					
LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ					
VN					
AU 9472440	A	19950103	(199521)		
EP 701557	A1	19960320	(199616)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
US 5525611	A	19960611	(199629)		27
JP 09501412	W	19970210	(199716)		95
EP 701557	A4	19970709	(199813)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9429308	A1	WO 1994-US6150	19940531
AU 9472440	A	AU 1994-72440	19940531
EP 701557	A1	EP 1994-921922	19940531
		WO 1994-US6150	19940531
US 5525611	A	US 1993-71648	19930604
JP 09501412	W	WO 1994-US6150	19940531
		JP 1995-501909	19940531
EP 701557	A4	EP 1994-921922	19940531

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9472440	A Based on	WO 9429308
EP 701557	A1 Based on	WO 9429308
JP 09501412	W Based on	WO 9429308

PRIORITY APPLN. INFO: US 1993-71648 19930604
AN 1995-036375 [05] WPIDS
CR 1997-362977 [33]; 1998-167941 [15]; 2000-205222 [18]; 2002-711569 [77]
AB WO 9429308 A UPAB: 20021204
Lavendamycin analogues of formula (I) and their salts are new. X = R10CONH
or R10CSNH; Y = H, OR11, SR11, N(R11)2, NR11N(R11)2, halo, NO2, CN,

R11C(=NR11), R12CO, R12CS or alkyl, aryl, cycloalkyl, alkynyl, alkenyl or heterocyclyl (all opt. substd.); R1 - R8 = H, halo, NO2, CN, OR13, SR13, N(R13)2, CON(R13)2, CSN(R13)2, COR13, CSR13, C(=NR13)R13 or alkyl, aryl, cycloalkyl, alkenyl, alkynyl or heteroalkyl, heterocyclyl, heteroalkenyl or heteroalkynyl (all opt. substd.); R9 = H, R12CO, R12CS or alkyl, cycloalkyl, aryl, alkenyl, alkynyl or heterocyclyl (all opt. substd.); R10, R11, R13 = H or alkyl, cycloalkyl, alkenyl, alkynyl, aryl or heterocyclyl (all opt. substd.); R12 = H, N(R11)2, OR11, SR11, NR11N(R11)2, OR14N(R11)2 or alkyl, cycloalkyl, aryl, alkenyl, alkynyl or heterocyclyl (all opt. substd.); and R14 = alkylene.

USE - (I) are useful as antitumour, antibacterial, antiviral and antiparasitic agents. They can be used to treat bacterial infections caused by both gram-positive and gram-negative bacteria such as Staphylococcus, Listerella, Salmonella and Mycobacterium. (I) are active against retroviruses such as HIV-1 and HIV-2, herpes viruses, hepatitis viruses, picorna viruses and pox viruses. (I) treat parasitic infections such as those caused by Amoeba, Babesia and Nosema. (I) are active against ovarian, colon, breast, stomach, pancreatic and skin tumours. In partic. (I) have been found to be selectively active against ras K tumour cells.

Dwg.0/0

ABEQ US 5525611 A UPAB: 19960724

A compound having the following formula (I), wherein, X is R10OCNH or R10SCNH, Y is H, OR11 SR11, N(R11)2, NR11N(R11)2, a halogen atom, NO2, CN, R11C(=NR11), R12CO, R12CS, or an alkyl, aryl, cycloalkyl, alkynyl, alkenyl or heterocyclic residue, said heterocyclic residue being selected from the group consisting of thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl**, and thiadiazolyl, each of said residues is unsubstituted or substituted with a single substituent selected from the group consisting of Rx, NH2, RxNH (Rx)2N, CN, N3, NO2, OH, halogen, SH, RxS, RxSO2, RxSO, RxO, COOH, COORx, CORx, CHO and CON (Rx)2, R4 and R6, which may be the same or different, each is independently H, a halogen atom, NO2, CN, OR13, SR13, N(R13)2, -C(=O)N(R13)2, C(=S)N(R13)2, C(=O)R13, C(=S)R13, C(=NR13)R13, an alkyl, aryl, cycloalkyl, alkenyl, alkynyl, or heterocyclic residue, said-alkyl residue optionally containing a heteroatom selected from the group consisting of oxygen, sulphur and nitrogen, said heterocyclic residue being selected from the group consisting of thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl**, and thiadiazolyl, each of said residues is unsubstituted or substituted with a single substituent selected from the group consisting of Rx, NH2, RxNH, (Rx)2N, CN, N3, NO2, OH, halogen, SH, RxS, RxSO2, RxSO, RxO, COOH, COORx, CORx, CHO and CON(Rx)2, R10, R11 and R13 which is the same or different, each is independently H or an alkyl, cycloalkyl, alkenyl, alkynyl, aryl or heterocyclic residue, said heterocyclic residue being selected from the group consisting of thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl**, and thiadiazolyl, each of said residues is unsubstituted or substituted with a single substituent selected from the group consisting of Rx, NH2, RxNH, (Rx)2N, CN, N3, NO2, OH, halogen, SH, RxS, RxSO2, RxSO, RxO, COOH, COORx, CORx, CHO and CON(Rx)2, R12 is H, N(R11)2, OR11, SR11, NR11N(R11)2, OR14N(R11)2, or an alkyl, cycloalkyl, aryl, alkenyl, alkynyl or heterocyclic residue, said heterocyclic residue being selected from the group consisting of thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl,

oxadiazolyl, and thiadiazolyl, each of said residues are unsubstituted or substituted with a single substituent selected from the group consisting of Rx, NH₂, RxNH, (Rx)₂N, CN, N₃, NO₂, OH, halogen, SH, RxS, RxSO₂, RxSO, RxO, COOH, COORx, CORx, CHO and CON(Rx)₂, and R₁₄ is an alkylene residue, Rx is an alkyl, cycloalkyl, aryl, alkenyl, alkynyl or heterocyclic residue, said heterocyclic residue being selected from the group consisting of thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isothiazolyl, isoxazolyl, thiazolyl, **oxadiazolyl**, and thiadiazolyl, or a pharmaceutically acceptable salt thereof.

Dwg.0/0

L17 ANSWER 20 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1993-336568 [42] WPIDS
 CROSS REFERENCE: 1997-131824 [12]
 DOC. NO. CPI: C1993-148850
 TITLE: New phenyl derivs. - useful as phosphodiesterase IV and tumour necrosis factor inhibitors.
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): CHRISTENSEN, S B; CHRISTENSEN, I S B
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 48
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9319749	A1	19931014	(199342)*	EN	45
RW: AT BE CH DE DK ES FR GB GR IE IT LI LU MC MW NL OA PT RU SD SE					
W: AU BB BG BR CA CZ FI HU JP KP KR LK MG MN NO NZ PL RO SK US					
ZA 9302264	A	19931124	(199402)		44
AU 9337910	A	19931108	(199408)		
NO 9403663	A	19941115	(199505)		
EP 633776	A1	19950118	(199507)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
FI 9404549	A	19941130	(199508)		
CZ 9402397	A3	19950517	(199528)		
SK 9401171	A3	19950607	(199532)		
EP 633776	A4	19950125	(199546)		
JP 07508508	W	19950921	(199546)		18
US 5552438	A	19960903	(199641)		18
NZ 251092	A	19961220	(199708)		
CN 1092406	A	19940921	(199716)		
TW 294652	A	19970101	(199716)		
US 5614540	A	19970325	(199720)		
AU 677776	B	19970508	(199727)		
HU 70523	T	19951030	(199732)		
US 5643946	A	19970701	(199732)		17
AU 9733229	A	19971023	(199750)		
SG 47107	A1	19980320	(199818)#		
CZ 283425	B6	19980415	(199821)		
BR 1100473	A3	19980422	(199822)		
NO 303116	B1	19980602	(199828)		
JP 2873090	B2	19990324	(199917)		26
EP 919544	A1	19990602	(199926)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
SK 279958	B6	19990611	(199930)		
AU 705566	B	19990527	(199932)		
MX 187418	B	19971210	(199936)		

AU 9936759 A 19990819 (199945)
 IL 105221 A 20000131 (200015)
 RU 2136656 C1 19990910 (200035)
 AU 724115 B 20000914 (200051)
 RO 115872 B1 20000728 (200052)
 EP 633776 B1 20010509 (200128) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 DE 69330206 E 20010613 (200141)
 ES 2157923 T3 20010901 (200161)
 PH 31379 A 19981029 (200254)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9319749	A1	WO 1993-US1991	19930305
ZA 9302264	A	ZA 1993-2264	19930330
AU 9337910	A	AU 1993-37910	19930305
NO 9403663	A	WO 1993-US1991	19930305
		NO 1994-3663	19940930
EP 633776	A1	EP 1993-907233	19930305
		WO 1993-US1991	19930305
FI 9404549	A	WO 1993-US1991	19930305
		FI 1994-4549	19940930
CZ 9402397	A3	CZ 1994-2397	19930305
SK 9401171	A3	WO 1993-US1991	19930305
		SK 1994-1171	19930305
EP 633776	A4	EP 1993-907233	
JP 07508508	W	JP 1993-517446	19930305
		WO 1993-US1991	19930305
US 5552438	A CIP of	US 1992-862030	19920402
	CIP of	US 1992-968762	19921030
		WO 1993-US1991	19930305
		US 1994-313094	19940929
NZ 251092	A	NZ 1993-251092	19930305
		WO 1993-US1991	19930305
CN 1092406	A	CN 1993-105725	19930402
TW 294652	A	TW 1993-104962	19930622
US 5614540	A CIP of	US 1992-862030	19920402
	CIP of	US 1992-968762	19921030
	CIP of	WO 1993-US1991	19930305
	Cont of	US 1994-313094	19940929
		US 1995-457942	19950518
AU 677776	B	AU 1993-37910	19930305
HU 70523	T	WO 1993-US1991	19930305
		HU 1994-2817	19930305
US 5643946	A CIP of	US 1992-862030	19920402
	CIP of	US 1992-968762	19921030
	Cont of	WO 1993-US1991	19930305
	Cont of	US 1994-313094	19940929
		US 1995-443636	19950518
AU 9733229	A Div ex	AU 1993-37910	19930305
		AU 1997-33229	19970808
SG 47107	A1	SG 1996-7903	19930305
CZ 283425	B6	WO 1993-US1991	19930305
		CZ 1994-2397	19930305
BR 1100473	A3	BR 1997-1100473	19970505
NO 303116	B1	WO 1993-US1991	19930305

JP 2873090	B2		NO 1994-3663	19940930
			JP 1993-517446	19930305
EP 919544	A1 Div ex		WO 1993-US1991	19930305
			EP 1993-907233	19930305
SK 279958	B6		EP 1998-204466	19930305
			WO 1993-US1991	19930305
AU 705566	B Div ex		SK 1994-1171	19930305
			AU 1993-37910	19930305
MX 187418	B		AU 1997-33229	19970808
AU 9936759	A Div ex		MX 1993-1943	19930402
			AU 1997-33229	19970808
IL 105221	A		AU 1999-36759	19990624
RU 2136656	C1		IL 1993-105221	19930330
			WO 1993-US1991	19930305
AU 724115	B Div ex		RU 1994-45291	19930305
			AU 1997-33229	19970808
RO 115872	B1		AU 1999-36759	19990624
			WO 1993-US1991	19930305
EP 633776	B1		RO 1994-1601	19930305
			EP 1993-907233	19930305
			WO 1993-US1991	19930305
		Related to	EP 1998-204466	19930305
DE 69330206	E		DE 1993-630206	19930305
			EP 1993-907233	19930305
ES 2157923	T3		WO 1993-US1991	19930305
PH 31379	A		EP 1993-907233	19930305
			PH 1993-45956	19930329

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9337910	A	Based on	WO 9319749
EP 633776	A1	Based on	WO 9319749
JP 07508508	W	Based on	WO 9319749
US 5552438	A	Based on	WO 9319749
NZ 251092	A	Based on	WO 9319749
US 5614540	A	Cont of	US 5552438
AU 677776	B	Previous Publ.	AU 9337910
		Based on	WO 9319749
HU 70523	T	Based on	WO 9319749
US 5643946	A	Cont of	US 5552438
CZ 283425	B6	Previous Publ.	CZ 9402397
		Based on	WO 9319749
NO 303116	B1	Previous Publ.	NO 9403663
JP 2873090	B2	Previous Publ.	JP 07508508
		Based on	WO 9319749
EP 919544	A1	Div ex	EP 633776
SK 279958	B6	Previous Publ.	SK 9401171
AU 705566	B	Div ex	AU 677776
		Previous Publ.	AU 9733229
AU 9936759	A	Div ex	AU 705566
RU 2136656	C1	Based on	WO 9319749
AU 724115	B	Div ex	AU 705566
		Previous Publ.	AU 9936759
RO 115872	B1	Based on	WO 9319749
EP 633776	B1	Related to	EP 919544
		Based on	WO 9319749

DE 69330206	E	Based on	EP 633776
		Based on	WO 9319749
ES 2157923	T3	Based on	EP 633776

PRIORITY APPLN. INFO: US 1992-968762 19921030; US 1992-862030
 19920402; US 1994-313094 19940929; US
 1995-457942 19950518; US 1995-443636 19950518
 ; SG 1996-7903 19930305

AN 1993-336568 [42] WPIDS

CR 1997-131824 [12]

AB WO 9319749 A UPAB: 20020823

Phenyl derivs. of formula (I), and their salts, are new: R1 = (CR4R5)nCOO(CR4R5)mR6, (CR4R5)nCONR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6, or (CR4R5)rR6, where all alkyl moieties are opt. substd. by halo; m = 0-2; n = 1-4; r = 1-6; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, furanyl, etc. 3-6C cycloalkyl, or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, where all cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me or one Et; X = YR2, halo, NO2, NR4R5, or formylamine; Y = O or S(O)m'; m' = 0-2; X2 = O or NR8; X3 = H or X; X4 = a gp. of formula (i) or (ii): X5 = H, R9, OR8, CN, COR8, COOR8, CONR8R8 or NR8R8; R2 = Me or Et, both opt. substd. by halo; s = 0-4; R3 = H, halo, 1-4C alkyl, CH2NHC(=O)CONH2, halo-substd. 1-4C alkyl, CH=CR8'R8', cyclopropyl (opt. substd. by R8'), CN, OR8, CH2OR8, NR8R10, CH2NR8R10, C(Z')H, COOR8, CONR8R10, or C=CR8'; Z' = O, NR9, NOR8, NCN, C(CN)2, CR8CN, CR8NO2, CR8COOR8, CR8CONR8R8, C(CN)NO2, C(CN)COOR9, or C(CN)NR8R8; Z = CY'R14, COOR14, CY'NR10R14, C(NR10)NR10R14, CN, C(NOR8)R14, C(NCN)SR9, etc. Het = 5-tetrazolyl, 2-, 4- or 5-imidazolyl, 5-imidazolidinyl, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-thiazolyl etc. The dotted line represents an opt. bond. Y' = O or S; R7 = (CR4R5)qR12 or 1-6C alkyl (where R12 or 1-6C alkyl are opt. substd. by one or more by Me or Et (themselves opt. substd. by 1-3F), F, Cl, Br, NO2, NR10R11, COR8, etc. q = 0, 1 or 2; R12 = 3-7C cycloalkyl, 2-, 3- or 4-pyridyl, pyrimidyl, pyrazolyl, 1- or 2-imidazolyl, thiazolyl, etc.; R8 = H or R9; R8' = R8 or F; R9 = 1-4C alkyl, opt. substd. by 1-3F; R10 = OR8 or R11; R11 = H or 1-4C alkyl (opt. substd. by 1-3F); or NR10R11 = a 5-7 membered ring contg. at least one additional heteroatom selected from O, N or S; R13 = oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl etc.; R14 = H or R7; or NR10R14 = a 5-7 membered ring contg. at least one additional heteroatom selected from O, N or S; (c) when n is 1 and m is 0, then R6 (in (CR4R5)nO(CR4R5)mR6) is not H; (d) when R12 is N-pyrazolyl, N-imidazolyl, N-triazolyl, N-pyrrolyl, N-piperazinyl, N-piperidinyl, or N-morpholinyl, then q is not 1; and (e) when X2R1 is OCF2H or OCF3, X is F, OCF2H or OCF3, X3 is H, s is O, X5 is H, Z is COOR14 and R14 is 1-7C unsubstd. alkyl, then R3 is not H.

USE/ADVANTAGE - (I) are useful as inhibitors of phosphodiesterase IV and are useful in treatment of allergic and inflammatory diseases such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis etc. (I) are also TNF inhibitors and thus useful in treatment of viral infections such as those caused by HIV-1, HIV-2, HIV-3, cytomegalovirus, adenovirus, influenza or **Herpes**, and animal viruses such as equine infectious anaemia virus, caprine arthritis virus, visna virus, maedi virus and other lentivirus. (I) may also be used to treat yeast and fungal infections, e.g., fungal meningitis. They may also be used to inhibit and/or reduce the toxicity of antifungal, antiviral and antibacterial agents.

Dwg.0/0

ABEQ US 5552438 A UPAB: 19961011

A compound of Formula (I), wherein: R1 is (CR4R5)nC(O)O(CR4R5)mR6, (CR4R5)nC(O)NR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6, or (CR4R5)rR6; m is 0 to 2; n is 1 to 4; r is 0 to 6; R4 and R5 are hydrogen or a C1-2 alkyl; R6 is hydrogen, methyl, hydroxyl, aryl, halo substituted aryl, aryloxy C 1-3 alkyl, halo substituted aryloxy C1-3 alkyl, indanyl, indenyl, C7-11 polycycloalkyl; X is YR2, halogen, nitro, NR4R5, or formyl amine; Y is O or S(O)m'; m' is 0-2; X2 is O or NR8; X3 is hydrogen or X; X4 is (a) or (b); X5 is H, R9, OR8, CN, C(O)R8, C(O)OR8, C(O)NR8R8, or NR8R8; R2 is CH3 and -CH2CH3; s is 0 to 4; R3 is CN; Z' is O, NR9, NOR8, NCN, C(-CN)2, C(-CN)NO2, C(-CN)C(O)OR9, or C(-CN)C(O)NR8R8; Z is C(Y')R14, C(O)OR14, C(Y')NR10R14, C(NR10)NR10R14, CN, C(NOR8)R14, C(NCN)NR10R14, C(NCN)SR9, (2-, 4- or 5-imidazolyl), (3-, 4- or 5-pyrazolyl), (4- or 5-triazolyl (1,2,3)), (3- or 5-triazolyl(1,2,4)), (5-tetrazolyl), (2-, 4- or 5-oxazolyl), (3-, 4- or 5-isoxazolyl), (3- or 5-oxadiazolyl (1,2,4)); the dotted line in formula (a) represents a single or double bond; Y' is O or S; R7 is -(CR4R5)qR12 or C1-6 alkyl wherein the R12 or C1-6 alkyl group is optionally substituted by C1-2 alkyl, -F, -Br, -Cl, NO2, -NR10R11, -C(O)R8, -C(O)OR8, -OR8, -CN, -C(O)NR10R11, -OC(O)NR10R11, -OC(O)R8, -NR10C(O)NR10R11, -NR10C(O)C(O)NR10R11, -NR10C(O)C(O)R10, thiazolyl, imidazolyl, oxazolyl, pyrazolyl, triazolyl, or tetrazolyl; q is 0-2; R12 is C3-C7-cycloalkyl, (2-, 3- or 4-pyridyl), pyrimidyl, pyrazolyl, (1- or 2-imidazolyl), thiazolyl, triazolyl, pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, (2- or 3-thienyl), (4- or 5-thiazolyl), quinolinyl, naphthyl, or phenyl; R8 is hydrogen or R9; R8, is R8 or fluorine; R9 is C1-4 alkyl; R10 is OR8 or R11; R11 is hydrogen, or C1-4 alkyl optionally substituted by one to three fluorines; R13 is oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, **oxadiazolyl**, or thiadiazolyl, and each of these heterocyclic rings is connected through a carbon atom and each may be unsubstituted or substituted by one or two C1-2 alkyl groups; R14 is hydrogen; or the pharmaceutically acceptable salts thereof.

Dwg. 0/0

ABEQ US 5614540 A UPAB: 19970516

Phenyl derivs. of formula (I), and their salts, are new: R1 = (CR4R5)nCOO(CR4R5)mR6, (CR4R5)nCONR4(CR4R5)mR6, (CR4R5)nO(CR4R5)mR6, or (CR4R5)rR6, where all alkyl moieties are opt. substd. by halo; m = 0-2; n = 1-4; r = 1-6; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, furanyl, etc. 3-6C cycloalkyl, or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, where all cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me or one Et; X = YR2, halo, NO2, NR4R5, or formylamine; Y = O or S(O)m'; m' = 0-2; X2 = O or NR8; X3 = H or X; X4 = a gp. of formula (i) or (ii): X5 = H, R9, OR8, CN, COR8, COOR8, CONR8R8 or NR8R8; R2 = Me or Et, both opt. substd. by halo; s = 0-4; R3 = H, halo, 1-4C alkyl, CH2NHC(=O)CONH2, halo-substd. 1-4C alkyl, CH=CR8'R8', cyclopropyl (opt. substd. by R8'), CN, OR8, CH2OR8, NR8R10, CH2NR8R10, C(Z')H, COOR8, CONR8R10, or C=CR8'; Z' = O, NR9, NOR8, NCN, C(CN)2, CR8CN, CR8NO2, CR8COOR8, CR8CONR8R8, C(CN)NO2, C(CN)COOR9, or C(CN)NR8R8; Z = CY'R14, COOR14, CY'NR10R14, C(NR10)NR10R14, CN, C(NOR8)R14, C(NCN)SR9, etc. Het = 5-tetrazolyl, 2-, 4- or 5-imidazolyl, 5-imidazolidinyl, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-thiazolyl etc. The dotted line represents an opt. bond. Y' = O or S; R7 = (CR4R5)qR12 or 1-6C alkyl (where R12 or 1-6C alkyl are opt. substd. by one or more by Me or Et (themselves opt. substd. by 1-3F), F, Cl, Br, NO2, NR10R11, COR8, etc. q = 0, 1 or 2; R12 = 3-7C cycloalkyl, 2-, 3- or 4-pyridyl, pyrimidyl, pyrazolyl, 1- or 2-imidazolyl, thiazolyl, etc.; R8 = H or R9; R8' = R8 or

F; R9 = 1-4C alkyl, opt. substd. by 1-3F; R10 = OR8 or R11; R11 = H or 1-4C alkyl (opt. substd. by 1-3F); or NR10R11 = a 5-7 membered ring contg. at least one additional heteroatom selected from O, N or S; R13 = oxazolidinyl, ozazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl etc.; R14 = H or R7; or NR10R14 = a 5-7 membered ring contg. at least one additional heteroatom selected from O, N or S; (c) when n is 1 and m is 0, then R6 (in (CR4R5)nO(CR4R5)mR6) is not H; (d) when R12 is N-pyrazolyl, N-imidazolyl, N-triazolyl, N-pyrrolyl, N-piperazinyl, N-piperidinyl, or N-morpholinyl, then q is not 1; and (e) when X2R1 is OCF2H or OCF3, X is F, OCF2H or OCF3, X3 is H, s is O, X5 is H, Z is COOR14 and R14 is 1-7C unsubstd. alkyl, then R3 is not H.

USE/ADVANTAGE - (I) are useful as inhibitors of phosphodiesterase IV and are useful in treatment of allergic and inflammatory diseases such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis etc. (I) are also TNF inhibitors and thus useful in treatment of viral infections such as those caused by HIV-1, HIV-2, HIV-3, cytomegalovirus, adenovirus, influenza or **Herpes**, and animal viruses such as equine infectious anaemia virus, caprine arthritis virus, visna virus, maedi virus and other lentivirus. (I) may also be used to treat yeast and fungal infections, e.g., fungal meningitis. They may also be used to inhibit and/or reduce the toxicity of antifungal, antiviral and antibacterial agents.

ABEQ US 5643946 A UPAB: 19970806

A cpd. of formula (I) and its salt is new:

R1 = e.g. -(CR4R5)nC(O)O(CR4R5)mR6;

m = 0-2;

n = 1-4;

r = 0-6;

R4,R5 = H or a 1-2C alkyl;

R6 = H, methyl, hydroxyl, aryl, halo substituted aryl, aryloxy 1-3C alkyl, etc.;

provided that:

e.g. (a) when R6 is hydroxyl, then m is 2;

X = YR2, halogen, nitro, NR4R5, or formyl amine;

Y = O or S(O)m';

m' = 0-2;

X2 = O or NR8;

X3 = H or X;

X4 = a gp. of formula (a) or (b):

X5 = H, R9, OR8, CN, C(O)R8, C(O)OR8, C(O)NR8R8, or NR8R8;

R2 = -CH3 and -CH2CH3 optionally substituted by 1 or more halogens;

s = 0-4;

R3 = cyclopropyl optionally substituted by R8';

Z = C(Y')R14, C(O)OR14, C(Y')NR10R14, etc.;

the dotted line in formula (a) represents a single or double bond;

Y' = O or S;

R7 = e.g. -(CR4R5)qR12;

q = 0-2;

R12 = e.g. 3-7C-cycloalkyl;

R8 = H or R9;

R8' = R8 or fluorine;

R9 = 1-4C alkyl optionally substituted by one to three fluorines;

R10 = OR8 or R11;

R11 = H or 1-4C alkyl optionally substituted by one to three fluorines; or when R10 and R11 are as NR10R11 they may together with the nitrogen form a 5-7 membered ring optionally containing at least one additional heteroatom selected from O/N/or S;

R13 = e.g. oxazolidinyl;
 R14 = H or R7; or when R10 and R14 are as NR10R14 they may together with the nitrogen form a 5 to 7 membered ring optionally containing one or more additional heteroatoms selected from O, N, or S; provided that:

e.g. when R12 is e.g. N-pyrazolyl then q is not 1.
 Dwg.0/0

L17 ANSWER 21 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1993-336567 [42] WPIDS
 CROSS REFERENCE: 1993-386067 [48]; 1996-009476 [01]; 1997-288607 [26]
 DOC. NO. CPI: C1993-148849
 TITLE: New cyclohexane-ylidene derivs. - useful for inhibiting prodn. of tumour necrosis factor and treating allergic and inflammatory diseases.
 DERWENT CLASS: B03 B05
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; FORSTER, C J; CHRISTENSEN, I S B
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 43
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9319748	A1	19931014 (199342)*	EN	28	
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW					
NL NO NZ PL RO RU SD SE SK US					
AU 9337383	A	19931108 (199408)			
AU 9338079	A	19931108 (199408)			
ZA 9302261	A	19941130 (199502)		56	
EP 633775	A1	19950118 (199507)	EN		
R: BE CH DE FR GB IT LI NL					
EP 636025	A1	19950201 (199509)	EN		
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 07508262	W	19950914 (199545)		11	
EP 633775	A4	19950222 (199611)			
EP 636025	A4	19950222 (199611)			
CN 1092407	A	19940921 (199716)			
AU 708544	B	19990805 (199943)			
EP 633775	B1	20000531 (200031)	EN		
R: BE CH DE FR GB IT LI NL					
DE 69328778	E	20000706 (200039)			
EP 636025	B1	20010718 (200142)	EN		
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 3195353	B2	20010806 (200147)		13	
DE 69330459	E	20010823 (200156)			
ES 2158860	T3	20010916 (200164)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9319748	A1	WO 1993-US1990	19930305
AU 9337383	A	AU 1993-37383	19930305
AU 9338079	A	AU 1993-38079	19930312
ZA 9302261	A	ZA 1993-2261	19930330
EP 633775	A1	EP 1993-906297	19930305

EP 636025	A1	WO 1993-US1990	19930305
		EP 1993-907493	19930312
		WO 1993-US2325	19930312
JP 07508262	W	JP 1993-517445	19930305
		WO 1993-US1990	19930305
EP 633775	A4	EP 1993-906297	
EP 636025	A4	EP 1993-907493	
CN 1092407	A	CN 1993-105726	19930402
AU 708544	B Div ex	AU 1993-38079	19930312
		AU 1996-71999	19961126
EP 633775	B1	EP 1993-906297	19930305
		WO 1993-US1990	19930305
DE 69328778	E	DE 1993-628778	19930305
		EP 1993-906297	19930305
		WO 1993-US1990	19930305
EP 636025	B1	EP 1993-907493	19930312
		WO 1993-US2325	19930312
JP 3195353	B2	JP 1993-517445	19930305
		WO 1993-US1990	19930305
DE 69330459	E	DE 1993-630459	19930312
		EP 1993-907493	19930312
		WO 1993-US2325	19930312
ES 2158860	T3	EP 1993-907493	19930312

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9337383	A	Based on	WO 9319748
AU 9338079	A	Based on	WO 9319750
EP 633775	A1	Based on	WO 9319748
EP 636025	A1	Based on	WO 9319750
JP 07508262	W	Based on	WO 9319748
AU 708544	B	Div ex	AU 675640
		Previous Publ.	AU 9671999
EP 633775	B1	Based on	WO 9319748
DE 69328778	E	Based on	EP 633775
		Based on	WO 9319748
EP 636025	B1	Based on	WO 9319750
JP 3195353	B2	Previous Publ.	JP 07508262
		Based on	WO 9319748
DE 69330459	E	Based on	EP 636025
		Based on	WO 9319750
ES 2158860	T3	Based on	EP 636025

PRIORITY APPLN. INFO: US 1992-968753 19921030; US 1992-862083
19920402; WO 1993-US2045 19930305

AN 1993-336567 [42] WPIDS

CR 1993-386067 [48]; 1996-009476 [01]; 1997-288607 [26]

AB WO 9319748 A UPAB: 20011105

Cyclohexane-ylidene derivs. of formula (I), and their pharmaceutically acceptable salts, are new. R1 = -(CR4R5)nC(O)O((CR4R5)mR6, -(CR4R5)nC(O)NR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6 or -(CR4R5)rR6; where alkyl moieties are opt. substd. with 1 or more halogen; m = 0-2; n = 1-4; r = 1-6; R4, R5 = H or 1-2C alkyl; R6 = H, Me, OH, aryl, opt. halo-substd., aryloxy (1-3C) alkyl) opt. halo-substd., indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, pyranal, tetrahydrothienyl, thienyl, tetrahydrothiopyranal, thiopyranal,

3-6C cycloalkyl or 4-6C cycloalkyl contg. 1 or 2 unsatd. bonds, where cycloalkyl and heterocyclic moieties are opt. substd. with 1-3 Me or one Et; provided that: a) when R6=OH, then m = 2; or b) when R6 = OH, then r = 2-6; or c) when R6 = 2-tetrahydropyranyl, 2-tetrahydrothiopyranyl, 2-tetrahydrofuranyl, or 2-tetrahydrothienyl, then m = 1 or 2; or d) when R6 = as for (c), then r = 1-6; e) when n = 1 and m = 0, then R6 is other than H in -(CR4R5)nO(CR4R5)mR6; X = YR2, halogen, NO2, NR4R5 or formyl amine; Y = O or S(O)m'; m' = 0-2; X2 = 0 or NR8; X3 = H or X; R2 = Me or Et opt. substd. by 1 or more halogen; s = 0-4; R3 = H, halogen, 1-4C alkyl opt. halo-substd., CH2NHC(O)C(O)NH2, -CH=CR8'R8', cyclopropyl opt. substd. by R8', CN, OR8, CH2OR8, NR8R10, CH2NR8R10, C(Z')H, C(O)OR8, C(O)NR8R10 or C=CR8'; Z' = O, NR9, NOR8, NCN, C(-CN)2, CR8CN, CR8NO2, CR8C(O)OR8, CR8C(O)NR8R8, C(-CN)NO2, C(-CN)C(O)OR9 or C(-CN)C(O)NR8R8; Z = C(-CN)2, CR14CN, CR14C(O)OR8, CR14C(O)NR8R14, C(-CN)NO2, C(-CN)C(O)OR9, C(-CN)OC(O)R9, C(-CN)OR9 or C(-CN)C(O)NR8R14; R7 = -(CR4R5)qR12 or 1-6C alkyl (where R12 and alkyl are opt. substd. by 1 or more Me or Et opt. substd. by 1-3 F), F, Br, Cl, NO2, -NR10R11, -C(O)R8, -CO2R8, -OR8, -CN, -C(O)NR10R11, -OC(O)NR10R11, -OC(O)R8, -NR10C(O)NR10R11, -NR10C(O)R11, -NR10C(O)OR9, -NR10C(O)R13, -C(NR10)NR10R11, -C(NCN)NR10R11, -C(NCN)SR9, -NR10C(NCN)SR9, -NR10C(NCN)NR10R11, -NR10S(O)2R9, -S(O)m'R9, -NR10C(O)C(O)NR10R11, -NR10C(O)C(O)R10,, thiazolyl, imidazolyl, oxazolyl, pyrazolyl, triazolyl or tetrazolyl; q = 0-2; R12 = 3-7C cycloalkyl; 2-, 3- or 4-pyridyl; pyrimidyl, pyrazolyl; 1- or 2-imidazolyl; thiazolyl; triazolyl; pyrrolyl, piperazinyl; piperidinyl,; morpholinyl; furanyl; 2- or 3-thienyl; 4- or 5-thiazolyl; quinolinyl; naphthyl; or Ph; R8 = H or R9; R8' = R8 or F; R9 = 1-4C alkyl opt. substd. by 1-3F; R10 = OR8 or R11; R11 = H or 1-4C alkyl opt. substd. by 1-3 F; or when R10 and R11 are NR10R11, they may together with N form a 5-7 membered ring opt. contg. at least one additional O, N or S; R13 = oxazolidinyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, **oxadiazolyl**, or thiadiazolyl, and each heterocyclic ring is connected through a C, and is opt. substd. by 1 or 2 1-2C alkyl; R14 = H or R7; or when R8 and R14 are as NR8R14 they may together with N forma 5-7 membered ring opt. contg. 1 or more additional O, N or S; provided that when R12 is N-pyrazolyl, N-imidazolyl, N-triazolyl, N-pyrrolyl, N-piperazinyl, N-piperidinyl or N-morpholinyl, then q is not 1.

USE - (I) inhibit cyclic nucleotide phosphodiesterase IV or the prodn. of Tumour Necrosis Factor nd are useful for treating allergic and inflammatory diseases (claimed) e.g. asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic or vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of myocardium and brain, chronic glomerulonephritis, endotoxic shock and adult respiratory distress syndrome, also diabetes insipidus and CNS disorders. (I) can also be used to treat viruses HIV-1,2 and 3, cytomegalovirus, influenza, adenovirus and **Herpes** viruses; also yeast and fungal infections, e.g. funal meningitis. (I) may also be used for inhibiting and/or reducing toxicity of anti-fungal, anti-bacterial or anti-viral agents e.g. Amphotericin B. Daily oral dosage is 0.001-100, pref. 0.01-40 mg/kg, in 1-6 doses.

Dwg.0/0

L17 ANSWER 22 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1993-336566 [42] WPIDS
 DOC. NO. CPI: C1993-148848
 TITLE: New phenyl-cyclohexane cpds. - useful as
 phosphodiesterase IV and tumour necrosis factor

inhibitors.
 DERWENT CLASS: B03 B05 C02 C03
 INVENTOR(S): CHRISTENSEN, S B; CHRISTENSEN, I S B
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 42
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9319747	A1	19931014	(199342)*	EN	30
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW					
NL NO NZ PL RO RU SD SE SK US					
AU 9337382	A	19931108	(199408)		
EP 634930	A1	19950125	(199508)	EN	
R: BE CH DE FR GB IT LI NL					
CN 1094711	A	19941109	(199544)		
JP 07508261	W	19950914	(199545)		12
EP 634930	A4	19950222	(199611)		
US 5602173	A	19970211	(199712)		12
JP 3195352	B2	20010806	(200147)		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9319747	A1	WO 1993-US1988	19930305
AU 9337382	A	AU 1993-37382	19930305
EP 634930	A1	EP 1993-906296	19930305
		WO 1993-US1988	19930305
CN 1094711	A	CN 1993-105721	19930402
JP 07508261	W	JP 1993-517444	19930305
		WO 1993-US1988	19930305
EP 634930	A4	EP 1993-906296	
US 5602173	A CIP of	US 1992-862112	19920402
	CIP of	US 1992-968760	19921030
		WO 1993-US1988	19930305
		US 1994-313096	19940929
JP 3195352	B2	JP 1993-517444	19930305
		WO 1993-US1988	19930305

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9337382	A Based on	WO 9319747
EP 634930	A1 Based on	WO 9319747
JP 07508261	W Based on	WO 9319747
US 5602173	A Based on	WO 9319747
JP 3195352	B2 Previous Publ.	JP 07508261
	Based on	WO 9319747

PRIORITY APPLN. INFO: US 1992-968760 19921030; US 1992-862112
 19920402; US 1994-313096 19940929

AN 1993-336566 [42] WPIDS

AB WO 9319747 A UPAB: 19931202

Cyclohexyl-phenyl derivs. of formula (I), and their salts, are new. In (I)
 R1 is (CR4R5)nC(O)O(CR4R5)mR6, (CR4R5)nC(O)NR4(CR4R5)mR6,

(CR4R5)nO(CR4R5)mR6, or (CR4R5)rR6, where all alkyl moieties are opt. substd. by halo; m is 0-2; n is 1-4; r is 1-6; R4, R5 are H or 1-2C alkyl; R6 is H, Me, OH, aryl or aryloxy(1-3C)alkyl (both opt. substd. by halo), indanyl, indenyl, 7-11C polycycloalkyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, furanyl, tetrahydropyranyl, pyranal, tetrahydrothienyl, thienyl, tetrahydrothiopyranal, thiopyranal, 3-6C cycloalkyl, or 4-6C cycloalkyl contg. 1-2 unsatd. bonds, where all cycloalkyl and heterocyclic gps. are opt. substd. by 1-3 Me, or one Et; X is YR2, halo, NO2, NR4R5, or formylamine; Y is O or S(O)m'; m' is 0-2; X2 is O or NR8; X3 is H or X; R2 is Me or Et, both opt. substd. by halo; s is 0-4; R3 is H, halo, 1-4C alkyl, CH2NHCOCNH2, etc.

USE/ADVANTAGE - (I) are useful as inhibitors of phosphodiesterase IV and thus useful in treatment of allergic and inflammatory diseases such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, and in treatment of diabetes insipidus and CNS disorders such as depression and multi-infarct dementia. (I) are also TNF inhibitors and thus useful in treatment of viral infections such as those caused by HIV-1, HIV-2, HIV-3, cytomegalovirus, adenovirus, influenza or **Herpes**, and animal viruses such as equine infectious anaemia virus, caprine arthritis virus, visna virus, maedi virus and other lentivirus. (I) may also be used to treat yeast and fungal infections, e.g., fungal meningitis. They may also be used to inhibit and/or reduced the toxicity of antifungal, antiviral and antibacterial agents.

Dwg.0/0

ABEQ US 5602173 A UPAB: 19970320

A cpd. of formula (I) or its salts: R1 = -(CR4R5)nC(O)O(CR4R5)mR6, -(CR4R5)nC(O)NR4(CR4R5)mR6, -(CR4R5)nO(CR4R5)mR6, or -(CR4R5)rR6; the alkyl moieties may be opt. substd. by one or more halo; m = 0 to 2; n = 1 to 4; r = 0 to 6; R4, R5 = H or 1-2C alkyl; R6 = H, methyl, hydroxy, aryl, halo substd. aryl, aryloxy 1-13C alkyl, halo substd. aryloxy 1-13C alkyl, indenyl, indenyl, 7-11C polycycloalkyl 3-6C cycloalkyl, or a 4-6C cycloalkyl contg. one or two unsatd. bonds, the cycloalkyl moiety may be opt. substd. by 1 to 3 methyl or one ethyl; provided that: a) when R6 = hydroxy, then m = 2; or b) when R6 = hydroxy, then r = 2 to 6; or c) when n = 1 and m = 0, then R6 is not H in -(CR4R5)nO(CR4R5)mR6; X = YR2, halo, nitro, NR4R5, or formyl amine; Y = O; m' = 0 - 2; X2 = O or NR8; X3 = hydrogen or X; R2 = -CH3 or -CH2CH3 opt. substd. by 1 or more halo; s = 0 - 4; R3 = CN; Z = CR8R8OR14, CR8R8OR15, CR8R8SR14, CR8R8SR15, CR8R8S(O)m'R7, CR8R8NR10R14, CR8R8NR10S(O)2NR10R14, CR8R8NR10S(O)2R7, CR8R8NR10C(Y')R14, CR8R8NR10C(O)OR7, CR8R8NR10C(Y')NR10R14, CR8R8NR10C(NCN)NR10R14, CR8R8NR10C(CR4NO2)NR10R14, CR8R8NR10C(NCN)SR9, CR8R8NR10C(CR4NO2)SR9, CR8R8C(O)OR14, CR8R8C(Y')NR10R14, CR8R8C(NR10)NR10R14, CR8R8CN, CR8R8(tetrazolyl), CR8R8(imidazolyl), CR8R8(imidazolidinyl), CR8R8(pyrazolyl), CR8R8(thiazolyl), CR8R8(thiazolidinyl), CR8R8(oxazolyl), CR8R8(oxazolidinyl), CR8R8(triazolyl), CR8R8(isoxazolyl), CR8R8(oxadiazolyl), CR8R8(thiadiazolyl), CR8R8(morpholinyl), CR8R8(piperidinyl), CR8R8(piperazinyl), CR8R8(pyrrolyl), CR8R8C(NOR8)R14, CR8R8C(NOR14)R8, CR8R8NR10C(NR10)SR9, CR8R8NR10C(NR10)NR10R14, CR8R8NR10C(O)C(O)NR10R14, or CR8R8NR10C(O)C(O)OR14; Y' = O; R7 = -(CR4R5)qR12 or 1-6C alkyl; R12 or 1-6C alkyl is opt. substd. by one or more 1-2C alkyl opt. substd. by 1-3 -F, -Br, -Cl, -NO2, -NR10R11, -C(O)R8, -C(O)OR8, -OR8, -CN, -C(O)NR10R11, -OC(O)NR10R11, -OC(O)R8, -NR10C(O)NR10R11, -NR10C(O)R11, -NR10C(O)OR9, -C(NR10)NR10R11, -C(NCN)NR10R11, -C(NCN)SR9, -NR10C(NCN)SR9,

-NR10C(NCN)NR10R11, -NR10S(O)2R9, -S(O)m'R9, -NR10C(O)C(O)NR10R11 or NR10C(O)C(O)R10; q = 0 - 2; R12 = 3-7C cycloalkyl, (2-, 3- or 4-pyridyl), pyrimidyl, pyrazolyl, (1- or 2-imidazolyl), thiazolyl, triazolyl, pyrrolyl, piperazinyl, piperidinyl, morpholinyl, furanyl, (2- or 3-thienyl), (4- or 5-thiazolyl), quinolinyl, naphthyl, or phenyl; R8 = H or R9; R8' = R8 or fluorine; R9 = 1-4C alkyl opt. substd. by 1-3 F; R10 = OR8 or R11; R11 = H, or 1-4C alkyl opt. substd. by 1-3 F; or NR10R11 = 5 to 7 membered ring opt. contg. at least one additional O, N, or S; R14 = H or R7; R15 = C(O)R14, C(O)NR4R14, S(O)2R7, or S(O)2NR4R14.
Dwg.0/0

L17 ANSWER 23 OF 23 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1993-134358 [16] WPIDS
 DOC. NO. CPI: C1993-059968
 TITLE: New pyrrolidinone(s) - inhibit TNF and phosphodiesterase IV in the prodn. treatment of allergies, inflammatory diseases etc..
 DERWENT CLASS: B03
 INVENTOR(S): BENDER, P E; CHRISTENSEN, S B; CHRISTENSEN, S B
 PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
 COUNTRY COUNT: 22
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9307141	A1	19930415	(199316)*	EN	44
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE					
W: AU CA JP KR US					
AU 9228690	A	19930503	(199334)		
ZA 9207787	A	19930825	(199339)		
PT 100947	A	19940228	(199412)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9307141	A1	WO 1992-US8611	19921002
AU 9228690	A	AU 1992-28690	19921002
ZA 9207787	A	ZA 1992-7787	19921009
PT 100947	A	PT 1992-100947	19920904

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9228690	A Based on	WO 9307141

PRIORITY APPLN. INFO: US 1992-916733 19920720; US 1991-776508
 19911011; US 1992-916713 19920720

AN 1993-134358 [16] WPIDS

AB WO 9307141 A UPAB: 19950626

Heterocyclic-3-phenylpyrrolidin-2-one derivs. of formula (I) and their salts are new. In the formula R1 = e.g. 1-12C alkyl (opt. substd. by halo), 3-6C cycloalkyl (opt. substd. by 1-3 Me or Et), 4-6C cycloalkenyl, 7-11C polycycloalkyl, etc.; X1 = O or S; X2 = O or NR14; X3 = H or X; X = YR2, halo, NO2, NR14R14 or formamide; Y = O or S(O)m; R2 = Me or Et opt. substd. by F; R3 = e.g. H, halo, CN, 1-4C alkyl (opt. substd. by halo), cyclopropyl (opt. substd.) etc.; R3' = e.g. H, halo, 1-4C alkyl (opt. halo

substd.), cyclopropyl (opt. substd.), etc.; A = 2-, 3-, or 4-pyridinyl, 4-morpholinyl or piperidinyl, 1-, 2-, 4-, or 5-imidazolyl, 2- or 3-thienyl, 2- or 5-pyrimidyl or 4- or 5-thiazolyl (all opt. substd.); R8 = H, 2-, 4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl-(1,2,3), 3- or 5-(triazolyl(1,2,4), 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-**oxadiazolyl**(1,2,4), 2-**oxadiazolyl**(1,3,4), 2-thiadiazolyl(1,3,4), 2-, 4- or 5-thiazolyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl, etc. (all opt. ring substd.); R14 = H or 1-12C alkyl (opt. halo substd.); m = 0-2; q = 0-1.

USE/ADVANTAGE - (I) inhibit phosphodiesterase IV and TNF and are used to treat e.g. allergic, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, chronic glomerulonephritis, endotoxic shock and adult respiratory distress syndrome. They also treat diabetes insipidus and CNS disorders such as depression and multiinfarct dementia. (I) also treat HIV (e.g. HIV-1, -2 and -3) ARC or any other disease associated with HIV infection. They treat viral infections such as cytomegalovirus, influenza, adenovirus and **herpes** viruses such as **Herpes** zoster and **Herpes** simplex. The cpds. also treat yeast and fungal infections e.g. fungal meningitis and candida infections. The cpds. may also inhibit and/or reduce the toxicity of antifungal, antibacterial or antiviral agents.

0/0

Dwg.0/0

ABEQ ZA 9207787 A UPAB: 19931123

Heterocyclic-3-phenylpyrrolidin-2-one derivs. of formula (I) and by halo), 3-6C cycloalkyl (opt. substd. by 1-3 Me or Et). 4-6C cycloalkenyl, 7-11C polycycloalkyl, etc.; X1 = O or S; X2 = O or NR14; X3 = H or X; X = YR2, halo, NO2, NR14R14 or formamide; Y = O or S(O)m; R2 = Me or Et opt. substd. by F; R3 = e.g. H, halo, CN, 1-4C alkyl (opt. substd. by halo), cyclopropyl (opt. substd.) etc.; R3' = e.g. H, halo, 1-4C alkyl (opt. halo substd.), cyclopropyl (opt. substd.), etc.; A = 2-, 3-, or 4-pyridinyl, 4-morpholinyl or piperidinyl, 1-, 2-, 4-, or 5-imidazolyl, 2- or 3-thienyl, 2- or 5-pyrimidyl or 4- or 5-thiazolyl (all opt. substd.); R8 = H, 2-, 4- or 5-imidazolyl, 3-, 4- or 5-pyrazolyl, 4- or 5-triazolyl-(1,2,3), 3- or 5-(triazolyl(1,2,4), 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 3- or 5-**oxadiazolyl**(1,2,4), 2-**oxadiazolyl**(1,3,4), 2-thiadiazolyl(1,3,4), 2-, 4- or 5-thiazolyl, 2-, 4- or 5-thiazolidinyl or 2-, 4- or 5-imidazolidinyl, etc. (all opt. ring substd.); R14 = H or 1-12C alkyl (opt. halo substd.); m = 0-2; q = 0-1.

USE/ADVANTAGE - (I) inhibits phosphodiesterase IV and tNF and are used to treat e.g. allergic, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, etc. They also treat diabetes insipidus and CNS disorders such as depression and multiinfarct dementia. (I) also treat HIV (e.g. HIV-1, -2 and -3) ARC or any other disease associated with HIV infection.